

- 499 -

phase chromatography (water/acetonitrile) to result in a white solid (0.8 g). MS and H-NMR were consistent with the proposed structure.

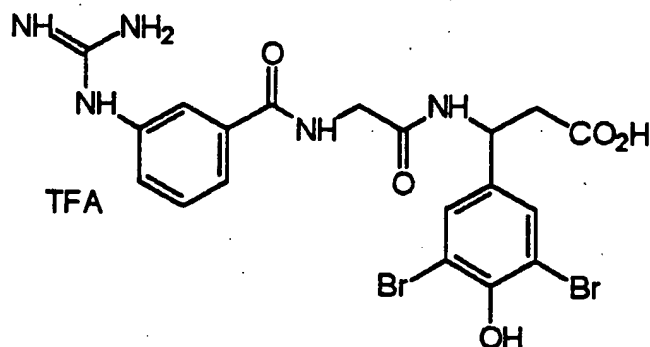
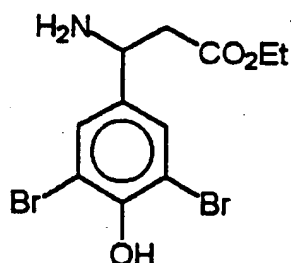
5 Step D

DL ethyl-3-amino-3-(3,5-diisopropoxyphenyl) propionate adduct produced in Step C (500mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 625 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

- 500 -

Example 276

Preparation of β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromo-4-hydroxybenzenepropanoic acid, trifluoroacetate salt

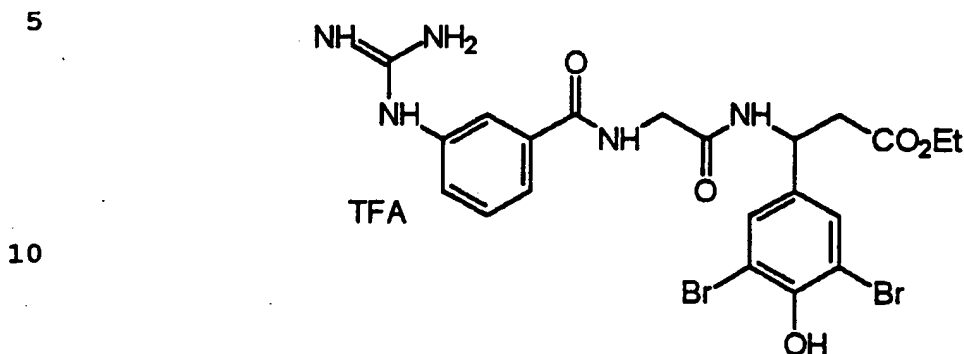
Step A

To 4-hydroxy-3,5-dibromobenzaldehyde (Aldrich) (10 g) in ethanol (70 mL) was added ammonium acetate (2.5 equivalents) followed by addition of ethyl hydrogen malonate (1.1 equivalents). The reaction mixture was stirred at reflux for 5 hours. The mixture was cooled, and ethanol removed under reduced pressure. Aqueous HCl (100 mL) was added and the mixture partitioned with ethyl acetate. The organic layer was discarded and the acid layer made basic with solid K_2CO_3 . The resulting mixture was partitioned between methylene chloride (150 mL), separated and dried over Na_2SO_4 . The solvent was evaporated to give DL ethyl-3-amino-3-(4-hydroxy-3,5-dibromophenyl) propionate as a solid and was collected by

- 501 -

filtration (1.3 g). MS and H-NMR were consistent with the proposed structure.

Step B



15 N,N'-disuccinimidyl carbonate (DSC) (1.0 g, 0.4 mmol) was added to the compound of Example M (1.0 g, 0.4 mmol) in dry dimethylformamide (6 mL) followed by addition of dimethylaminopyridine (100 mg). After a period of 20 minutes DL ethyl-3-amino-3-(4-hydroxy-3,5-dibromophenyl) propionate hydrochloride (1.1 g, 0.5 mmol) was added

20 followed by addition of NMM (2.0 mL). After complete reaction (1-16 hours) the product was purified by reverse phase chromatography (water/acetonitrile) to result in a white solid (.89 g). MS and H-NMR were consistent with the proposed structure.

25

Step C

DL ethyl-3-amino-3-(4-hydroxy-3,5-dibromophenyl) propionate adduct produced in Step B (500 mg) was dissolved in water/acetonitrile (1:1), followed by the

30 addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 425

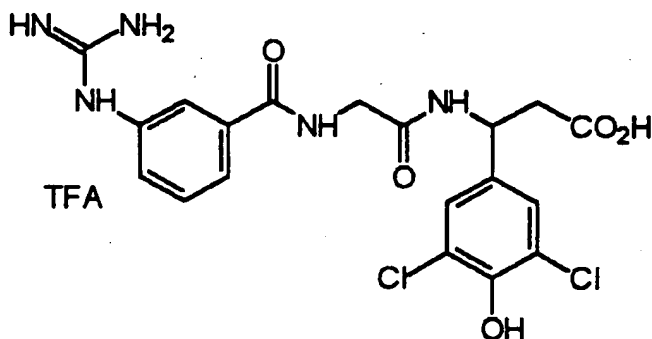
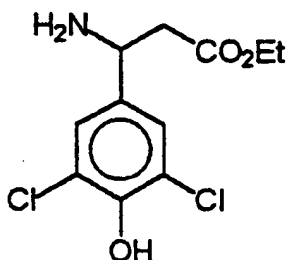
- 502 -

mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

- 503 -

Example 277

Preparation of β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichloro-4-hydroxybenzenepropanoic acid, trifluoroacetate salt

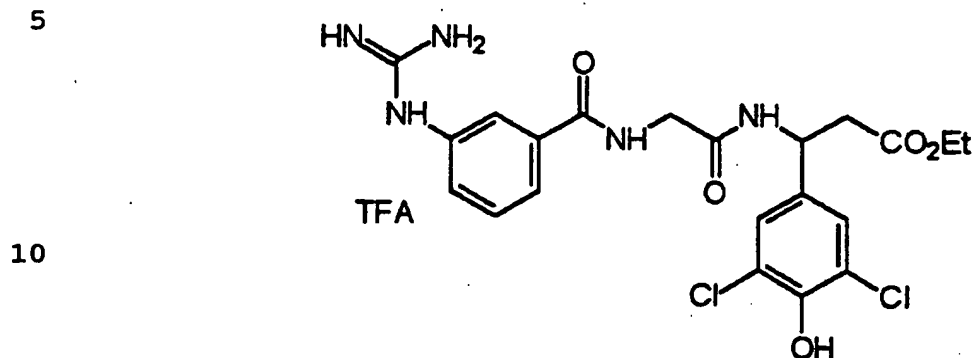
Step A

To 4-hydroxy-3,5-dichlorobenzaldehyde (Aldrich) (10 g) in ethanol (70 mL) was added ammonium acetate (2.5 equivalents) followed by addition of ethyl hydrogen malonate (1.1 equivalents). The reaction mixture was stirred at reflux for 5 hours. The mixture was cooled, and ethanol removed under reduced pressure. Aqueous HCl (100 mL) was added and the mixture partitioned with ethyl acetate. The organic layer was discarded and the acid layer made basic with solid K_2CO_3 . The resulting mixture was partitioned between methylene chloride (150 mL), separated and dried over Na_2SO_4 . The solvent was evaporated to give DL ethyl-3-amino-3-(4-hydroxy-3,5-

- 504 -

dichlorophenyl) propionate as solid (2.5 g). MS and H-NMR were consistent with the proposed structure.

Step B



15 N,N'-disuccinimidyl carbonate (DSC) (1.0 g, 0.4 mmol) was added to the compound of Example M (1.0 g, 0.4 mmol) in dry dimethylformamide (6 mL) followed by addition of dimethylaminopyridine (100 mg). After a period of 20 minutes DL ethyl-amino-3-(4-hydroxy-3,5-dichlorophenyl) propionate hydrochloride (1.1 g, 0.5 mmol) was added

20 followed by addition of NMM (2.0 mL). After complete reaction (1-16 hours) the product was purified by reverse phase chromatography (water/acetonitrile) to result in a white solid (0.9 g). MS and H-NMR were consistent with the proposed structure.

25

Step C

DL-ethyl-amino-3-(4-hydroxy-3,5-dichlorophenyl) propionate adduct prepared in Step B (500 mg) was dissolved in water/acetonitrile (1:1), followed by the

30 addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 325

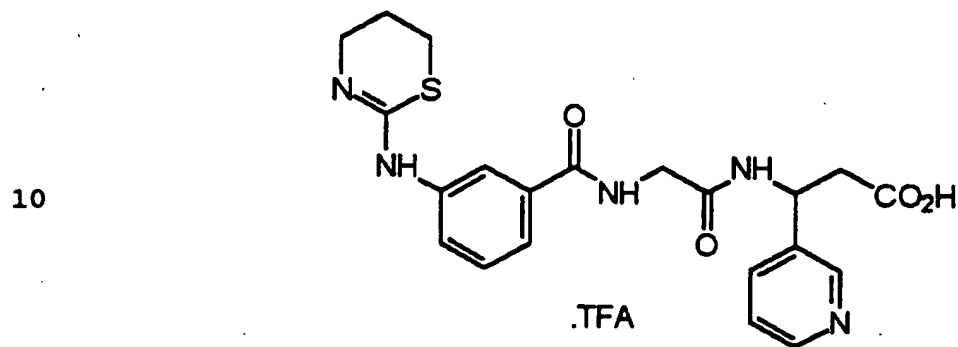
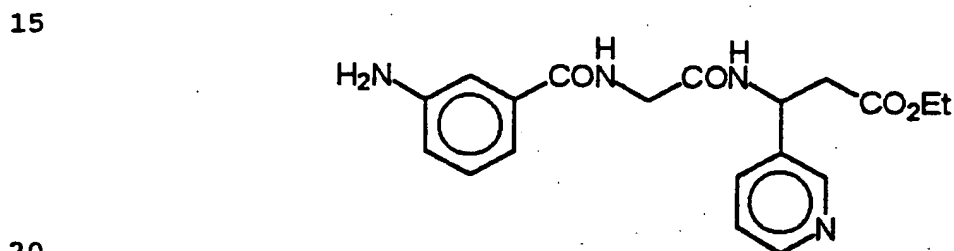
- 505 -

mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

- 506 -

Example 278

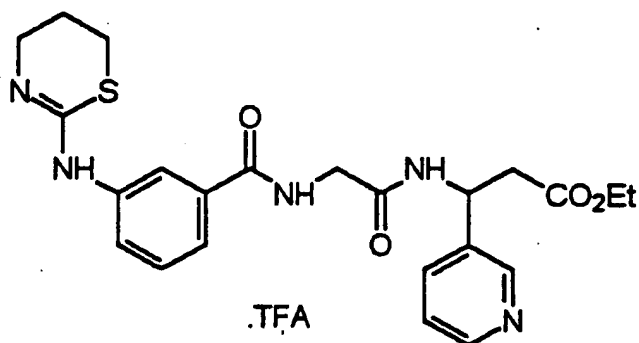
Preparation of β -[[2-[[[3-[(5,6-dihydro-4H-thiazin-2-yl) amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid, bis(trifluoroacetate) salt

Step A

The compound prepared in Example 104 (2.0 g) was added to absolute ethanol (60 mL) in a Parr jar. Palladium on carbon 5% (500 mg) was added and the mixture was hydrogenolyzed under 50 psi in a Parr apparatus for a period of 2.5 hours. After complete reaction the palladium catalyst was removed by filtration through a plug of celite. The solvent was removed under reduced pressure and the sample dried in vacuo.

30

- 507 -

Step B

The compound prepared in Step A was added to acetonitrile (20 mL) followed by addition of 2-methyl thiodihydro-1,3-thiazine (2.0 g) [prepared according to J. Chem. Soc. Perkin Transaction, 1943, p.243-245] and heated for 4 hours. After complete reaction water was added and the product was purified by reverse phase chromatography (water/acetonitrile) to result in a white solid (1.3 g). MS and H-NMR were consistent with the proposed structure.

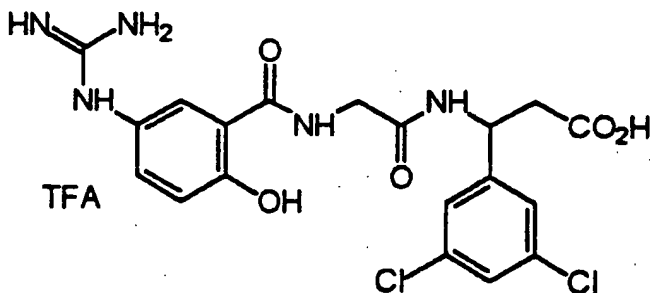
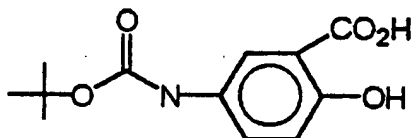
Step C

DL-ethyl 3-amino-3(pyridyl) propionate thiazine adduct prepared in Step B (700 mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 520 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

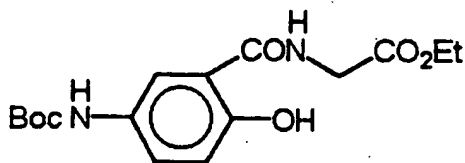
- 508 -

Example 279

Preparation of β -[[2-[[[5-[(aminoiminomethyl)amino]-2-hydroxyphenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid, trifluoroacetate salt

Step A

Amino salicylic acid (10 g), K_2CO_3 (10 g), and di-tert-butoxycarbonate (12 g) were placed in a flask containing water/acetonitrile (100 mL, (1:1)). The course of the reaction was monitored by RPHPLC. After complete reaction dilute aqueous HCl was added (pH = 4), the product was separated from mixture, and filtered resulting in a tan-red solid (15 g). The compound was dried in an oven at 70°C for 16 hours. MS and H-NMR were consistent with the proposed structure.

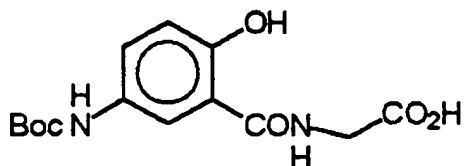
Step B

- 509 -

N,N'-disuccinimidyl carbonate (DSC) (2.0 g, 0.8 mmol) was added to the N-Boc compound produced in Step A (2.0 g, 0.4 mmol) in dry dimethylformamide (4 mL) followed by addition of dimethylaminopyridine (100 mg). After a period of 20 minutes, ethyl glycinate hydrochloride (2.1 g, 0.9 mmol) was added followed by addition of DIEA (2.0 mL). After complete reaction (2 hours) the product was extracted with ethyl acetate (100 mL) washed with aqueous HCl, brine and dried over Na₂SO₄ to give a dark oil (2.5 g). MS and H-NMR were consistent with the proposed structure.

Step C

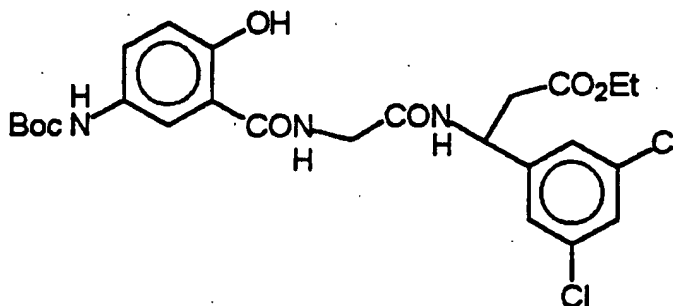
15



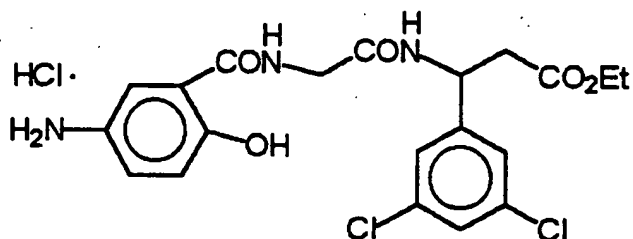
Ethyl glycinate N-Boc benzamide adduct produced in Step B (2.9 g) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (200 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) hydrochloric acid was added until pH = 4. The product was extracted with ethyl acetate (100 mL) washed with aqueous HCl, brine and dried over Na₂SO₄ to give a dark oil. The oil was vigorously stirred with ether to result in a solid (1.9 g) after filtration and dried in a vacuum oven for 16 hours. MS and H-NMR were consistent with the proposed structure.

30

- 510 -

Step D

10 N,N'-disuccinimidyl carbonate (DSC) (1.0 g, 0.4 mmol)
 was added to the glycine compound produced in Step C
 (1.0 g, 0.4 mmol) in dry dimethylformamide (6 mL) followed
 by addition of dimethylaminopyridine (100 mg). After a
 period of 20 minutes DL ethyl-3-amino-3-(3,5-
 15 dichlorophenyl) propionate hydrochloride (1.1 g, 0.5 mmol)
 was added followed by addition of NMM (2.0 mL). After
 complete reaction (1-16 hours) the product was purified by
 reverse phase chromatography (water/acetonitrile) to
 result in a white solid (0.9 g). MS and H-NMR were
 20 consistent with the proposed structure.

Step E

30 The compound produced in Step D (6 g) was dissolved
 in methylene chloride (50 mL). To this mixture
 HCl/dioxane (20 mL, 4N) was added. The mixture was
 stirred for 1-2 hours. The solvent was removed under
 reduced pressure followed by addition of ether. The

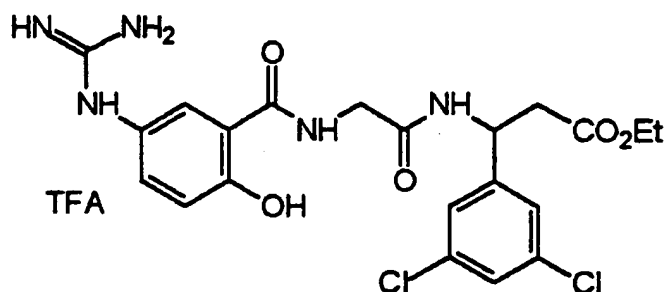
- 511 -

solvent was removed again under reduced pressure. The solid was purified by reverse phase chromatography (water/acetonitrile) to result in a white solid (0.8 g). MS and H-NMR were consistent with the proposed structure.

5

Step F

10



15

The aniline from step E was dissolved into acetonitrile (20 mL). To this mixture pyrazole carboxamidine hydrochloride (2 g) was added followed by addition of DIEA. The mixture was heated at reflux for 4 hours. After complete reaction (1-16 hours) the product was purified by reverse phase chromatography (water/acetonitrile) to result in a white solid (0.9 g). MS and H-NMR were consistent with the proposed structure.

20

Step G

25

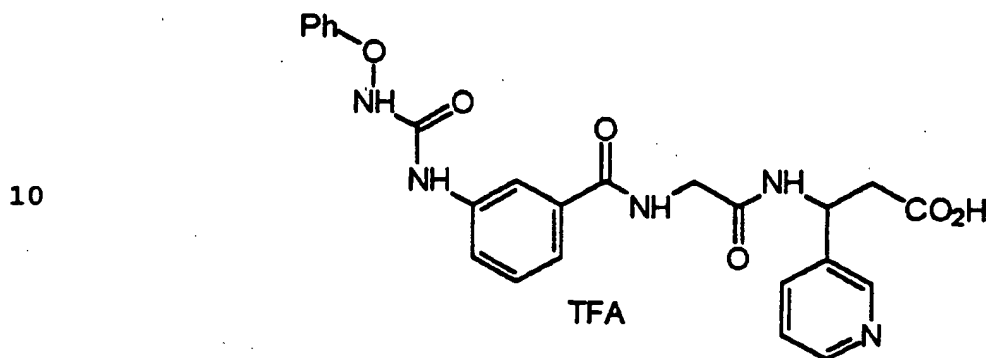
DL-ethyl 3-amino-3-(3,5-dichlorophenyl) propionate adduct produced in Step F (500 mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 125 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

30

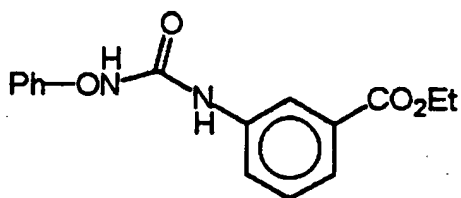
- 512 -

Example 280

Preparation of β -[[2-[[[3-[[(phenoxyamino)-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid, trifluoroacetate salt

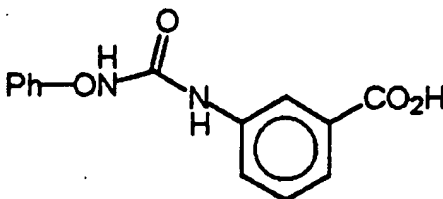
Step A

15

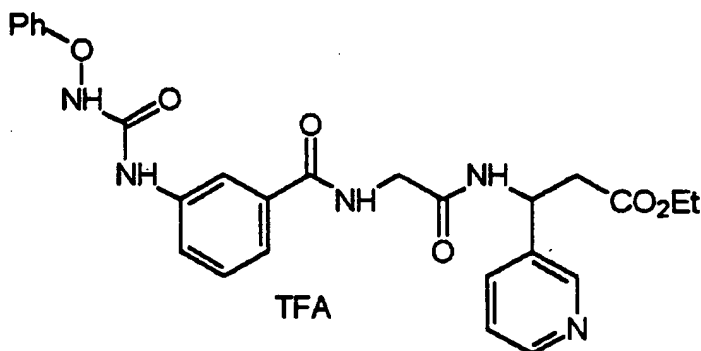


To O-phenyl hydroxyl amine hydrochloride (Fluka) (4 g) in acetonitrile was added 3-ethoxycarbonyl phenylisocyanate (Lancaster) (5 g) and NMM (1 equivalent). The reaction was stirred for 1 hour at 70°C. After complete reaction the solvent was removed under reduced pressure to give a solid mass. Water was added and a tan solid filtered (7.5 g). MS and H-NMR were consistent with the proposed structure.

- 513 -

Step B

The compound produced in Step A (7 g) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (4g). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (4-6 hours) 10% aqueous HCl was added until pH = 2. The product was filtered to give a white solid (7 g) which was dried in a vacuum oven at 70°C for 16 hours. MS and H-NMR were consistent with the proposed structure.

Step C

N,N'-disuccinimidyl carbonate (DSC) (1.4 g, 0.5 mmol) was added to the carboxylic acid-urea of O-phenyl hydroxyl amine produced in Step B and 3-ethoxycarbonyl phenylisocyanate [(A13) in Scheme V] (1.0 g, 0.5 mmol) in dry dimethylformamide (20 mL) followed by addition of dimethylaminopyridine (100 mg). After a period of 1 hour gly-DL-ethyl 3-amino-3-(pyridyl) propionate hydrochloride (2.2 g, 0.7 mmol) in DMF/NMM (1:1) (5.0 mL) was added in

- 514 -

on portion. After complete reaction the product was purified by reverse phase chromatography (water/acetonitrile) to result in a white solid (0.8 g). MS and H-NMR were consistent with the proposed structure.

5

Step D

The compound produced in Step C (300 mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 500 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

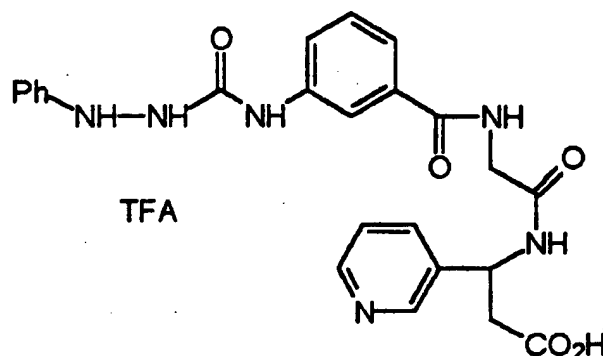
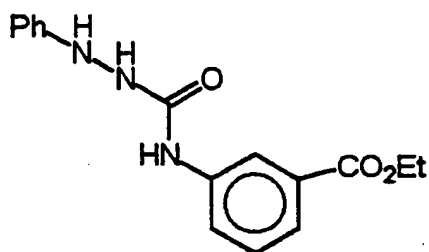
10

15

- 515 -

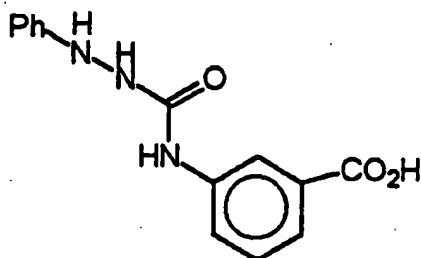
Example 281

Preparation of β -[[2-[[[3-[[[(ph nylamino)amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid, trifluoroacetate salt

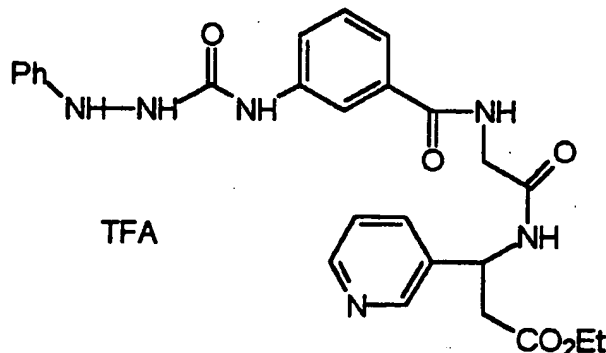
Step A

To phenyl hydrazine hydrochloride (Aldrich) (3.5 g) in acetonitrile was added 3-ethoxycarbonyl phenylisocyanate (Lancaster) (5 g) and NMM (1 equivalents). The reaction was stirred for 1 hour at 70°C. After complete reaction the solvent was removed under reduced pressure to give a solid mass. Water was added and the tan solid filtered (8.7 g). MS and H-NMR were consistent with the proposed structure.

- 516 -

Step B

The compound produced in Step A (5 g) was dissolved in water/acetonitrile (1:1), followed by the addition of sodium hydroxide (3 g). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (4-6 hours) 10% aqueous HCl was added until pH = 4. The product was filtered to give a yellow solid (3.2 g) and dried in a vacuum oven at 70°C for 16 hours. MS and H-NMR were consistent with the proposed structure.

Step C

N,N'-disuccinimidyl carbonate (DSC) (500 mg, 0.5 mmol) was added to the compound produced in Step B and 3-ethoxycarbonyl phenylisocyanate (1.0 g, 0.5 mmol) in dry dimethylformamide (20 mL) followed by addition of dimethylaminopyridine (100 mg). After a period of 1 hour glycine-DL-ethyl 3-amino-3-(pyridyl) propionate

- 517 -

hydrochloride (1.0 g, 0.7 mmol) in DMF/NMM (1:1) (5.0 mL) was added in one portion. After c mplet reaction the product was purified by reverse phase chromatography (water/acetonitrile) to result in a white solid (0.8g).

5 MS and H-NMR were consistent with the proposed structure.

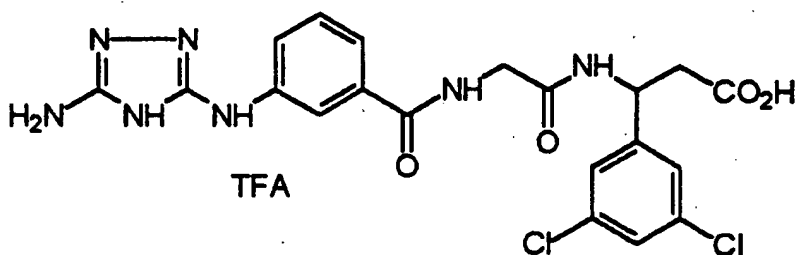
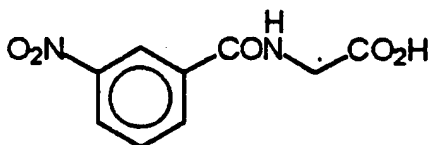
Step D

The compound produced in Step C (300 mg) was dissolved in water/acetonitrile (1:1), followed by the
10 addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse
15 phase chromatography (water/acetonitrile) to result in 500 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

- 518 -

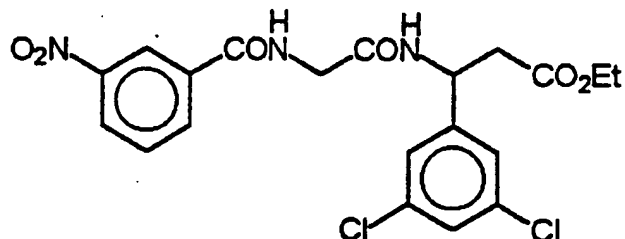
Example 282

Preparation of β -[[2-[[[3-[(5-amino-1,2,4-triazol-3-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-
dichlorobenzenepropanoic acid, trifluoroacetate salt

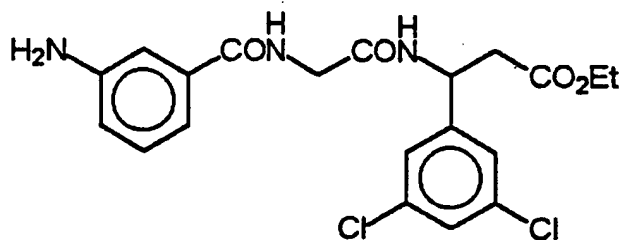
Step A

Glycine (20 g, 266 mmol) was added to water (200 mL), followed by addition of potassium hydroxide (20 g, 357 mmol) and the mixture cooled to 0°C in an ice bath. To this mixture 3-nitrobenzoyl chloride (Aldrich) (20 g, 108 mmol) was added in acetonitrile (20 mL) drop-wise over a 10 minute period. After complete reaction (3-4 hours) concentrated hydrochloric acid was added until pH=1 followed by addition of saturated aqueous NaCl (75 mL). The product was filtered, washed with water and air dried (22 g, 90% yield).

- 519 -

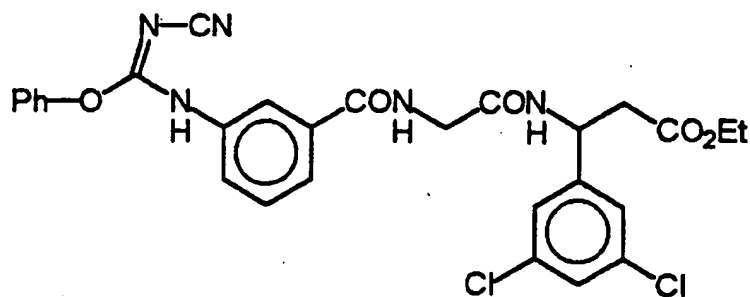
Step B

5
10
15
20
N,N'-disuccinimidyl carbonate (DSC) (1.5 g, 0.7 mmol) was added to the compound produced in Step A (1.0 g, 0.4 mmol) in dry dimethylformamide (6 mL) followed by addition of dimethylaminopyridine (100 mg). After a period of 20 minutes DL ethyl-3-amino-3-(3,5-dichlorophenyl) propionate hydrochloride (1.1 g, 0.5 mmol) was added followed by addition of NMM (2.0 mL). After complete reaction (1-16 hours) the product was isolated by adding water/aqueous HCl (5 ml) and filtering product to result in a white solid (0.9 g). MS and H-NMR were consistent with the proposed structure.

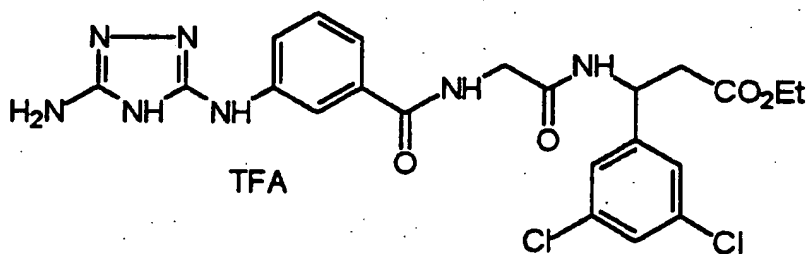
Step C

25
30
The compound produced in Step B was subjected to the conditions described in Tetrahedron Letters, Vol. 25 1984, 839-842 for the reduction of the nitro group. The reduction was preformed on 2 g of nitro compound.

- 520 -

Step D

10 To the compound produced in Step C (2 g) isopropanol (20 mL) was added followed by addition of diphenoxycyanamine (1 g) (Aldrich). The reaction was stirred for 1 hour at 70°C. After complete reaction the solvent was removed under reduced pressure to give a solid mass. Ether was added and the tan solid filtered (3.2 g). MS and H-NMR were consistent with the proposed structure.

Step E

25 To the compound produced in Step D (1 g) ethanol (10 mL) was added followed by addition of hydrazine (1.5 mL) (Aldrich). The reaction was stirred for 1 hour at 25°C. After complete reaction the solvent was removed under reduced pressure to give a solid mass. After complete reaction (1 hour) the product was purified by reverse phase chromatography (water/acetonitrile) to result in a white solid (0.7 g). MS and H-NMR were consistent with the proposed structure.

- 521 -

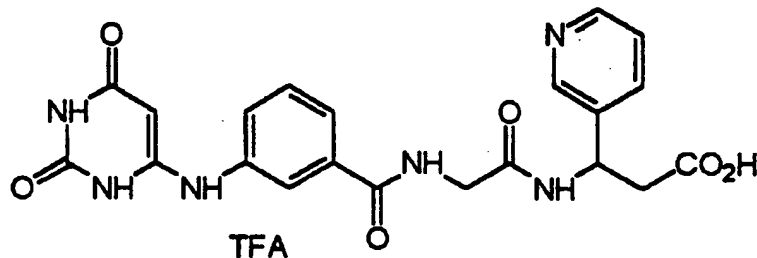
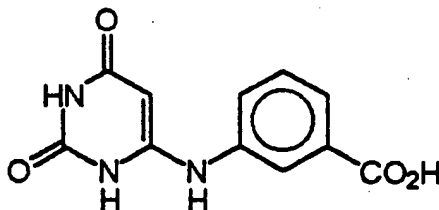
Step F

The compound produced in Step E (300 mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 430 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

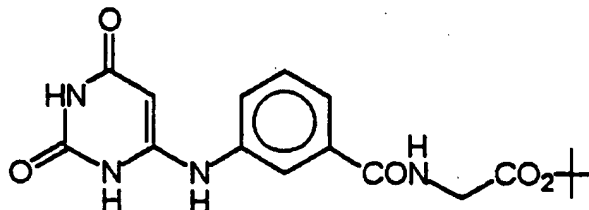
- 522 -

Example 283

Preparation of β -[[2-[[[3-[(1,2,3,4-tetrahydro-2,4-
dioxypyrimidin-6-yl)amino]phenyl]carbonyl]amino]-
5 acetyl]amino]pyridine-3-propanoic acid,
trifluoroacetate salt

15 Step A

20 3-Aminobenzoic acid (4 g) was added to ethoxyethanol (4 mL), followed by 6-chloro uracil (4 g), and heated to 125°C for 3-4 hours. The product was filtered, washed
25 with ether and air dried (4.5 g) to give a tan solid. MS and H-NMR were consistent with the proposed structure.

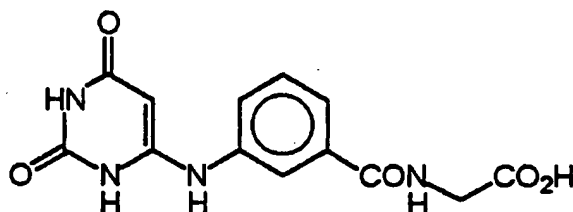
Step B

- 523 -

N,N'-disuccinimidyl carbonate (DSC) (2 g, 0.7 mmol) was added to the compound produced in Step A (2.0 g, 0.4 mmol) in dry dimethylformamide (6 mL) followed by addition of dimethylaminopyridine (100 mg). After a period of 20 minutes tert-butyl glycine hydrochloride (1.1 g, 0.5 mmol) was added followed by addition of DIEA (2.0 mL). After complete reaction (2-3 hours) the product was isolated by extraction in ethyl acetate, washed with aqueous HCl, saturated K_2CO_3 , brine and dried over Na_2SO_4 to result in a yellow oil (3 g). MS and H-NMR were consistent with the proposed structure.

Step C

15

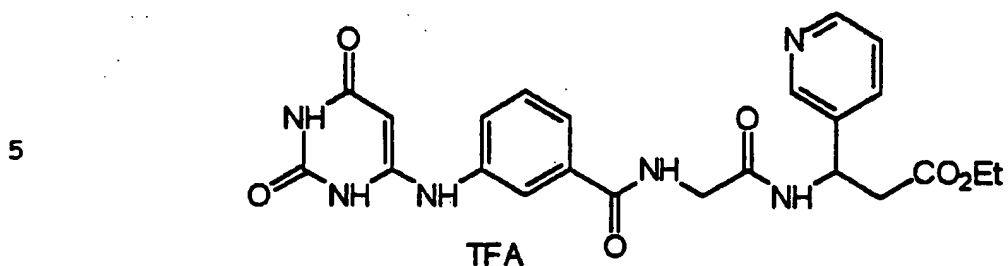


20

The compound produced in Step B (2 g) was dissolved in methylene chloride (50 mL). To this mixture TFA (20 mL) was added. The mixture was stirred for 12 hours. The solvent was removed under reduced pressure followed by addition of ether. The solid (1.8 g) was filtered and dried in a vacuum for 1-2 hours. MS and H-NMR were consistent with the proposed structure.

25

- 524 -

Step D

10 N,N'-disuccinimidyl carbonate (DSC) (1.5 g, 0.7 mmol) was added to the compound produced in Step C of Example 283 (1.0 g, 0.4 mmol) in dry dimethylformamide (6 mL) followed by addition of dimethylaminopyridine (100 mg). After a period of 20 minutes, DL ethyl-3-amino-3-(3-pyridyl) propionate hydrochloride (1.1 g, 0.5 mmol) was

15 added followed by addition of NMM (2.0 mL). After complete reaction (1-16 hours) the product was purified by reverse phase chromatography (water/acetonitrile) to result in a white solid (0.9 g). MS and H-NMR were consistent with the proposed structure.

20

Step E

The compound produced in Step D (300 mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was

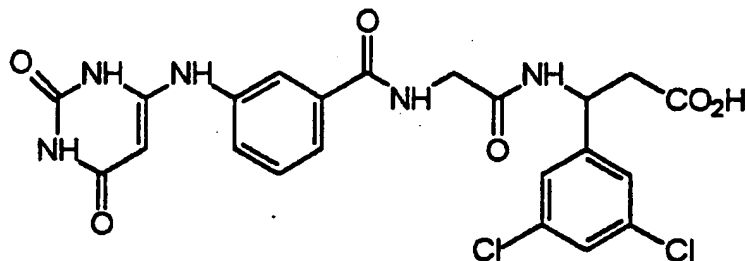
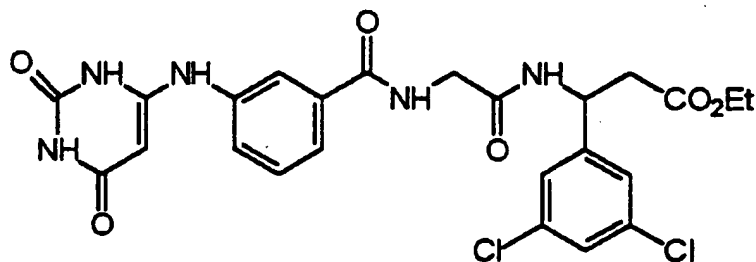
25 allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 430 mg of the title compound as a white solid. MS and H-NMR

30 were consistent with the proposed structure.

- 525 -

Example 284

Preparation of 3,5-dichloro- β -[[2-[[[3-[[1,2,3,4-tetrahydro-2,4-dioxypyrimidin-6-yl)amino]phenyl]-carbonyl]amino]acetyl]amino]benzenepropanoic acid

Step A

N,N'-disuccinimidyl carbonate (DSC) (0.6 g) was added to the compound from Step C of Example 283 (0.6 g,) in dry dimethylformamide (6 mL) followed by addition of dimethylaminopyridine (100 mg). After a period of 20 minutes DL ethyl-3-amino-3-(3,5-dichlorophenyl) propionate hydrochloride (1.1 g, 0.5 mmol) was added followed by addition of NMM (2.0 mL). After complete reaction (1-16 hours) the product was purified by reverse phase chromatography (water/acetonitrile) to result in a white solid (0.9 g). MS and H-NMR were consistent with the proposed structure.

- 526 -

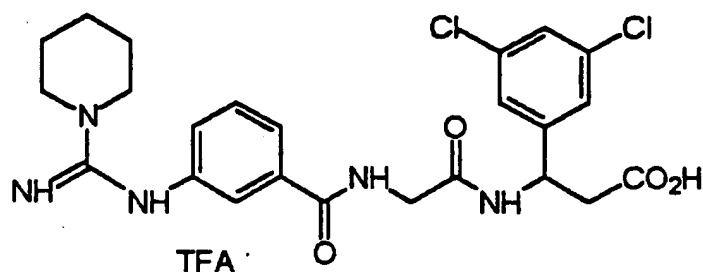
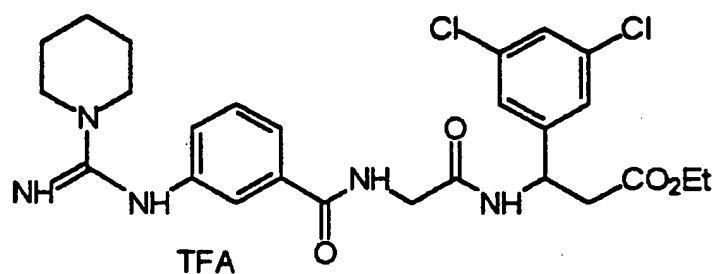
Step B

Th c mpound pr duced in Step A (200 mg) was dissolved in water/acetonitrile (1:1), followed by addition of lithium hydroxide (100 mg). The reaction was
5 allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 105
10 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

- 527 -

Example 285

Preparation of 3,5-dichloro- β -[[2-[[[3-[[imino(1-
piperidinyl)methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]benzenepropanoic acid,
trifluoroacetate salt

Step A

The above compound was prepared according to methodology of Example 24, substituting one equivalent of piperidine for benzylamine in Example 23, Step B, and an equivalent amount of DL ethyl-3-amino-3-(3,5-dichlorophenyl) propionate hydrochloride for DL ethyl-3-amino-3-(3-pyridyl) propionate dihydrochloride in Example 1, Step C and further used in Example 1, Step D as described in Example 23, Step C. MS and H-NMR were consistent with the proposed structure.

- 528 -

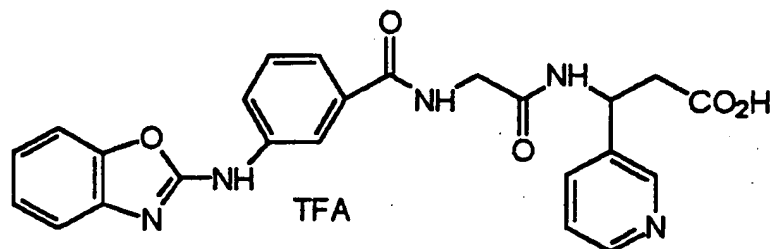
Step B

The compound prepared in Step A (200 mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was
5 allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 105
10 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

- 529 -

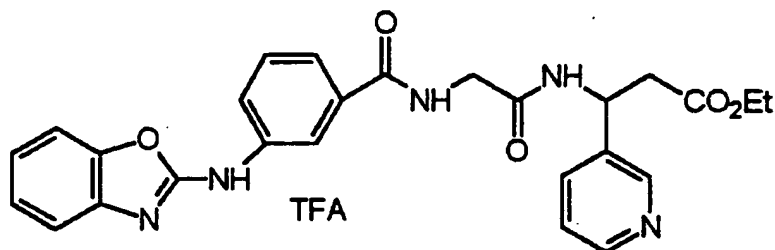
Example 286

Preparation of β -[[2-[[[3-[[benzoxazol-2-yl)amino]-phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid, trifluoroacetate salt

Step A

The compound prepared in Example 104 (2.0 g) was added to absolute ethanol (60 mL) in a Parr jar.

Palladium on carbon 5% (500 mg) was added and the mixture was hydrogenolyzed under 50 psi in a Parr apparatus for a period of 2.5 hours. After complete reaction the palladium catalyst was removed by filtration through a plug of celite. The solvent was removed under reduced pressure and the sample dried in vacuo.

Step B

The compound prepared in Step A was dissolved in DMF (20 mL). To this mixture 2-chlorobenzoxazole (Aldrich) (2 g) and K₂CO₃ (4 g) was added. The mixture was heated to 70°C until the aniline was consumed. After complete reaction, the product was purified by reverse phase

- 530 -

chromatography (water/acetonitrile) to result in 215 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

5 Step C

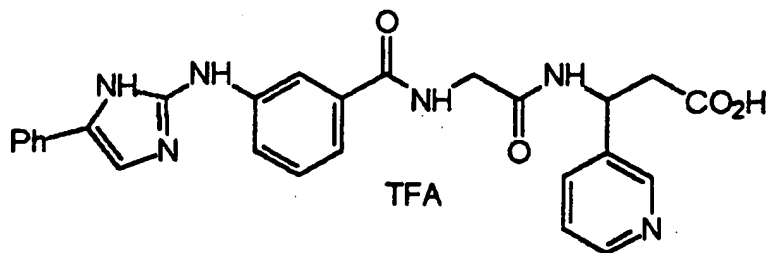
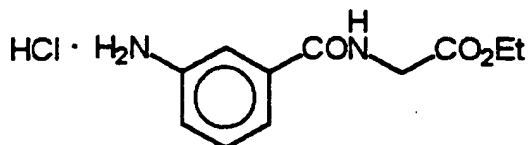
 The compound prepared in Step B (200 mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After
10 complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 185 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

15

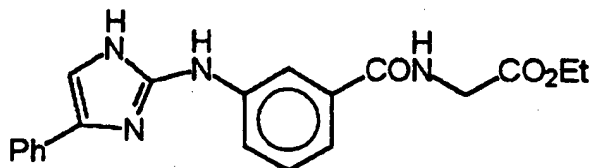
- 531 -

Example 287

Preparation of β -[[2-[[[3-[[5-phenyl-1H-imidazol-2-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-
propanoic acid, trifluoroacetate salt

Step A

The compound prepared in Example M, Step B (5 g) was added to ethanol (100 mL) followed by dry HCl in dioxane (10 mL). The mixture was heated to reflux for 2 hours. The solvent was removed under reduced pressure to give the ethyl ester (5.6 g). MS and H-NMR were consistent with the proposed structure.

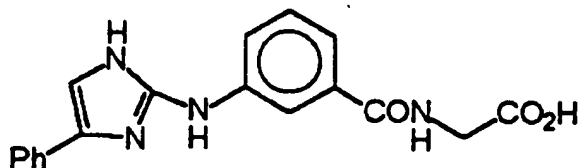
Step B

To the product of Step A (3 g) acetonitrile (50 mL) was added followed by addition of bromoacetophenone (2.7 g) and DIEA (2 mL). The mixture was heated for 2 hours and the solvent removed under reduced pressure. The

- 532 -

product was isolated by extraction into ethyl acetate and dried over Na_2SO_4 to give a dark red solid (5 g). MS and H-NMR were consistent with the proposed structure.

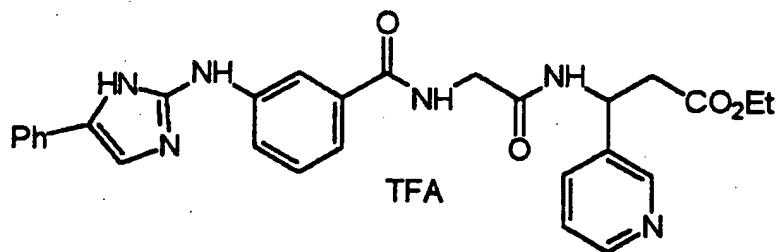
5 Step C



10

The compound produced in Step B (2 g) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) aqueous HCl was added until pH = 7. The product was filtered and dried in an oven to result in 2.6 g of a tan solid. MS and H-NMR were consistent with the proposed structure.

20 Step D



25

N,N'-disuccinimidyl carbonate (DSC) (0.3 g, 0.7 mmol) was added to the compound produced in Step C (0.5 g, 0.4 mmol) in dry dimethylformamide (5 mL) followed by addition of dimethylaminopyridine (100 mg). After a period of 20 minutes, DL ethyl-3-amino-3-(3-pyridyl) propionate hydrochloride (1.1 g, 0.5 mmol) was added followed by addition of NMM (2.0 mL). After complete reaction (1-16 hours) the product was purified by reverse phase chromatography (water/acetonitrile) to result in a white

- 533 -

solid (0.9 g). MS and H-NMR were consistent with the proposed structure.

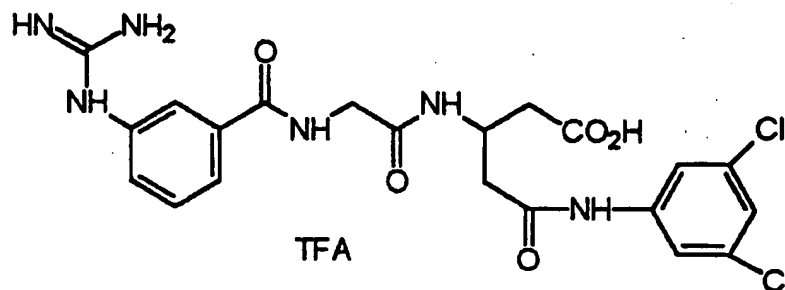
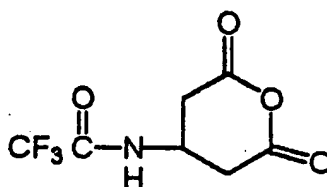
Step E

5 The compound produced in Step D (250 mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was
10 added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 110 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

- 534 -

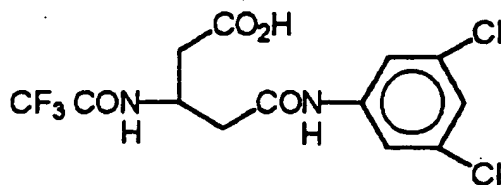
Example 288

Preparation of 3-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-5-[(3,5-
dichlorophenyl)amino]-5-oxopentanoic
acid, trifluoroacetate salt

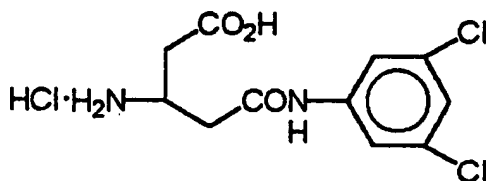
Step A

A mixture of β -amino glutaric acid (Sigma) (5.9 g) and trifluoroacetic anhydride (Sigma) (20 mL) was stirred for 1-2 hours at 25°C. The solvent was removed under reduced pressure to leave an oil. To the oil was added ether (50 mL) and the product filtered (5 g). MS and H-NMR were consistent with the proposed structure.

- 535 -

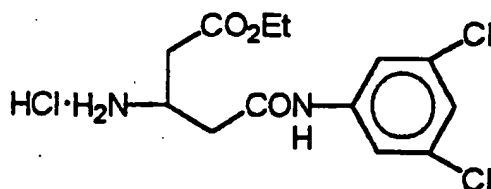
Step B

A DMF (20 mL) mixture of the product from Step A and 3,5 dichloroaniline (6 g) was stirred for 16 hours. After complete reaction aqueous HCl (100 mL) and ethyl acetate (100 mL) were added and the mixture, shaken and separated. The organic layer was washed with brine and dried over Na_2SO_4 to give the acid amide (4 g). MS and H-NMR were consistent with proposed structure.

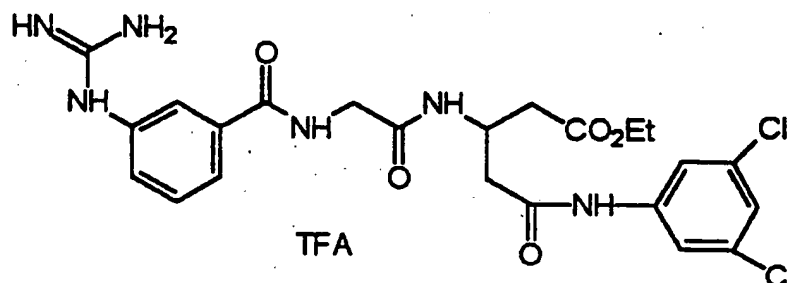
Step C

The trifluoroacetate group of the product of Step B was removed by heating the compound produced in Step B with dilute ammonium hydroxide (10 mL in 50 mL water). After complete reaction the mixture was acidified with 10% HCl and the product (2.5 g) was filtered. MS and H-NMR were consistent with the proposed structure.

- 536 -

Step D

The compound produced in Step C (2 g) was added to ethanol (100 mL) followed by dry HCl in dioxane (10 mL). The mixture was heated to reflux for 2 hours. The solvent was removed under reduced pressure to give the ethyl ester (1.9 g). MS and H-NMR were consistent with the proposed structure.

15 Step E

N,N-disuccinimidyl carbonate (DSC) (0.6 g, 0.7 mmol) was added to the compound produced in Example M, Step A (0.6 g, 0.4 mmol) in dry dimethylformamide (5 mL) followed by addition of dimethylaminopyridine (100 mg). After a period of 20 minutes the compound produced in Step D of Example 288 (0.7 g, 0.5 mmol) was added followed by addition of NMM (2.0 mL). After complete reaction (1-16 hours) the product was purified by reverse phase chromatography (water/acetonitrile) to result in a white solid (0.51 g). MS and H-NMR were consistent with the proposed structure.

- 537 -

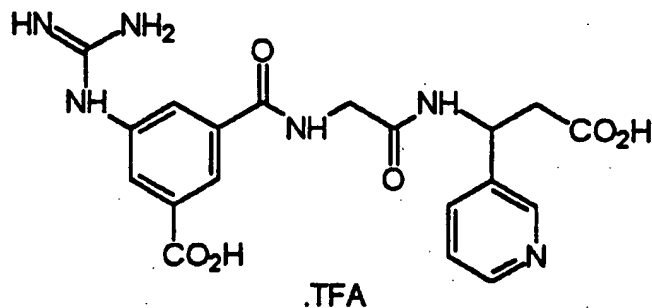
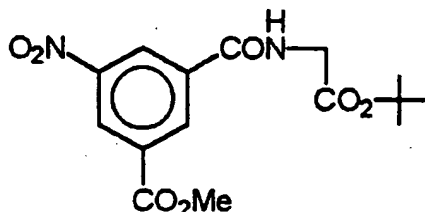
Step F

The compound produced in Step E (250 mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 110 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

- 538 -

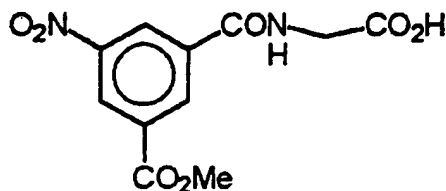
Example 289

Preparation of β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxyphenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid, bis(trifluoroacetate) salt

Step A

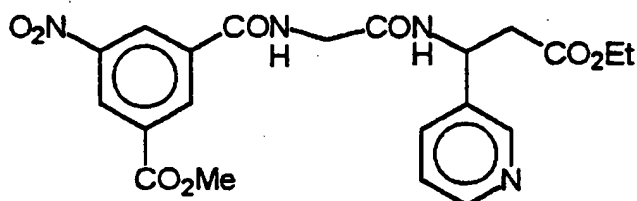
N,N' -disuccinimidyl carbonate (DSC) (6.5 g) was added to methyl hydrogen 5-nitroisophthalate (5 g) in dry dimethylformamide (10 mL) followed by addition of dimethylaminopyridine (200 mg). After a period of 20 minutes tert-butyl β -glycine (2.6 g) was added followed by addition of NMM (2.0 mL). After complete reaction (4 hours) the product was isolated by extraction into ethyl acetate and dried over Na_2SO_4 to result in a white solid (5.1 g). MS and H-NMR were consistent with the proposed structure.

- 539 -

Step B

5

The compound produced in Step A (5 g) was dissolved in dioxane (50 mL). To this mixture dry HCl (20 mL, 4N) was added. The mixture was stirred for 1-2 hours. The solvent was removed under reduced pressure followed by addition of ether and removal of the solvent under reduced pressure. The solid was filtered to result in a white solid (4 g) and dried in a vacuum oven. MS and H-NMR were consistent with the proposed structure.

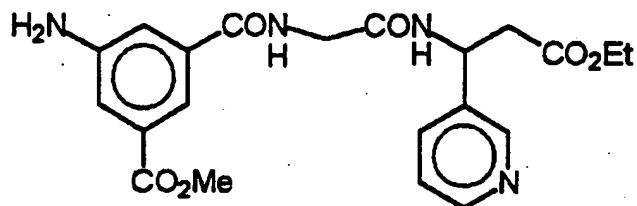
Step C

20

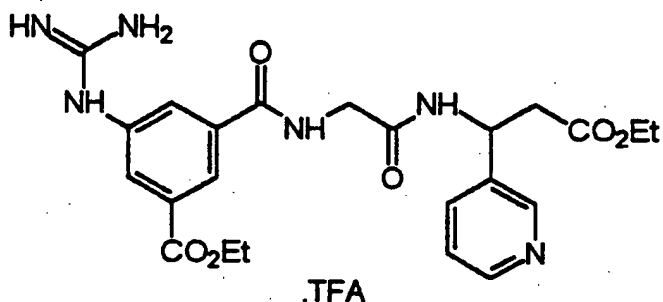
N,N-disuccinimidyl carbonate (DSC) (2 g) was added to the compound produced in Step B (2 g) in dry dimethylformamide (10 mL) followed by addition of dimethylaminopyridine (200 mg). After a period of 20 minutes, DL ethyl-3-amino-3-(3-pyridyl) propionate hydrochloride (1.6 g) was added followed by addition of NMM (2.0 mL). After complete reaction (4 hours) the product was isolated by extraction into ethyl acetate and dried over Na₂SO₄ to result in an oil (3 g). MS and H-NMR were consistent with the proposed structure.

30

- 540 -

Step D

The compound produced in Step C was subjected to the conditions described in Tetrahedron Letters, Vol. 25, 1984, 839-842 to reduce the nitro group. The reduction was performed on 2 g of nitro compound to give 1 g of product. MS and H-NMR were consistent with the proposed structure.

Step E

.TFA

The compound produced in Step D was guanidated according to the method in Example M on a 1 g scale and purified by reverse phase chromatography (water/acetonitrile) to result in 110 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

Step F

The compound produced in Step E (100 mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After

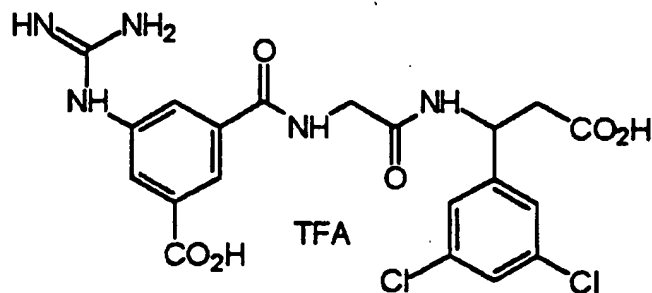
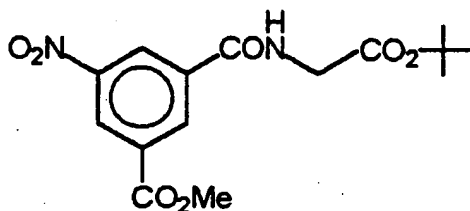
- 541 -

complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitril) to result in 110 mg of the title compound as a white solid. MS and H-NMR
5 were consistent with the proposed structure.

- 542 -

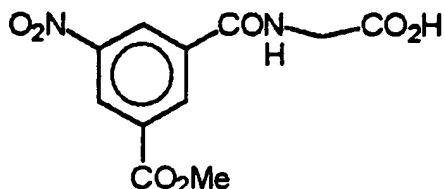
Example 290

Preparation of β -[[2-[[[3-[(amin iminomethyl)amino]-
5-carboxyphenyl]carbonyl]amino]acetyl]amino]-3,5-
5 dichlorobenzenepropanoic acid, trifluoroacetate salt

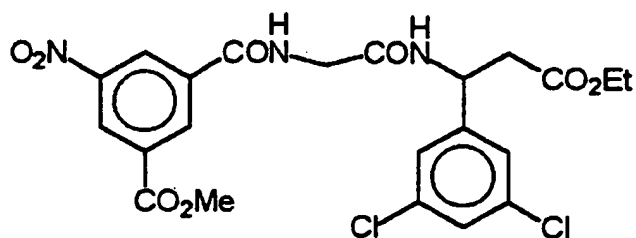
Step A

N,N-disuccinimidyl carbonate (DSC) (65 g) was added
to methyl hydrogen 5-nitroisophthalate (5 g) in dry
dimethylformamide (10 mL) followed by addition of
dimethylaminopyridine (200 mg). After a period of 20
25 minutes tert-butyl β -glycine (2.6 g) was added followed by
addition of NMM (2.0 mL). After complete reaction
(4 hours) the product was isolated by extraction into
ethyl acetate and dried over Na₂SO₄ to result in a white
solid (5.1 g). MS and H-NMR were consistent with the
30 proposed structure.

- 543 -

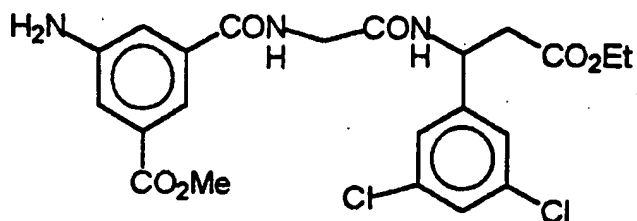
Step B

5
10
15
The compound produced in Step A (5 g) was dissolved in dioxane (50 mL). To this mixture dry HCl (20 mL, 4N) was added. The mixture was stirred for 12 hours. The solvent was removed under reduced pressure followed by addition of ether and removal of the solvent under reduced pressure. The solid was filtered to result in a white solid (4 g) and dried in a vacuum oven. MS and H-NMR were consistent with the proposed structure.

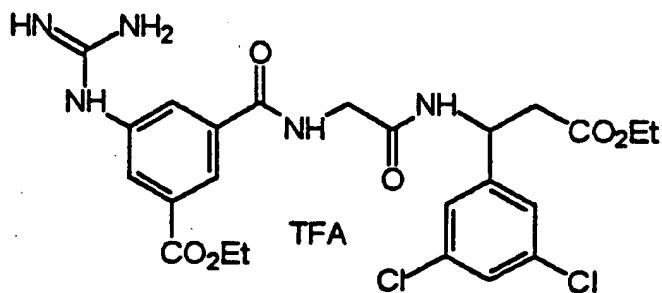
Step C

20
25
30
N,N'-disuccinimidyl carbonate (DSC) (2 g) was added to the compound produced in Step B (2 g) in dry dimethylformamide (10 mL) followed by addition of dimethylaminopyridine (200 mg). After a period of 20 minutes DL-ethyl 3-amino-3-(3,5-dichlorophenyl)propionate hydrochloride (1.6 g) was added followed by addition of NMM (2.0 mL). After complete reaction (4 hours) the product was isolated by extraction into ethyl acetate and dried over Na₂SO₄ to result in an oil (3 g). MS and H-NMR were consistent with the proposed structure.

- 544 -

Step D

The compound produced in Step C was subjected to the conditions discribed in Tetrahedron Letters, Vol. 25, 1984, 839-842 to reduce the nitro group. The reduction was performed on 2g of nitro compound to give 1 g of product.

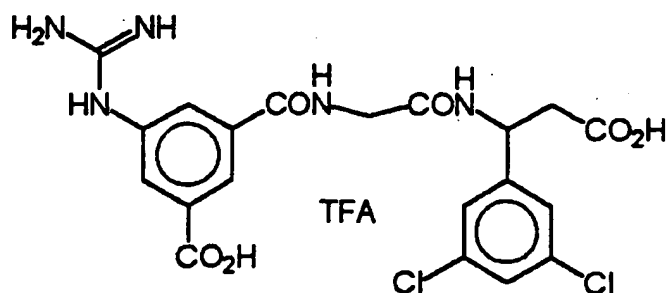
Step E

The compound produced in Step D was guanidated according to the method in Example M on a 1 g scale and purified by reverse phase chromatography (water/acetonitrile) to result in 110 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

- 545 -

Step F

5



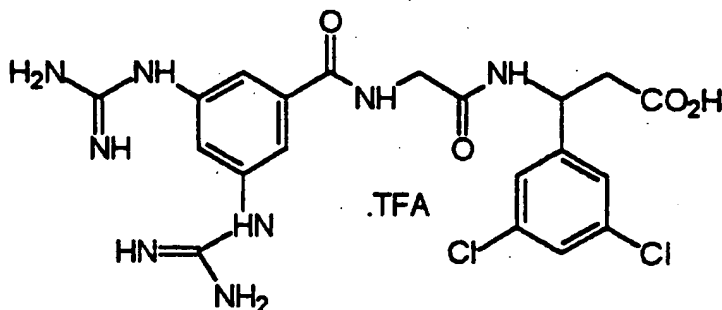
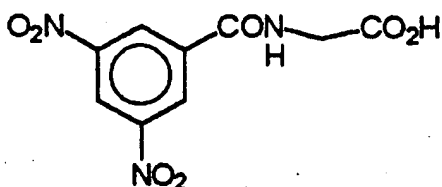
10 The compound produced in Step E (100 mg) was
dissolved in water/acetonitrile (1:1), followed by the
addition of lithium hydroxide (100 mg). The reaction was
allowed to stir at 25°C, and monitored by HPLC. After
complete hydrolysis (1-2 hours) trifluoroacetic acid was
15 added until pH = 2. The product was purified by reverse
phase chromatography (water/acetonitrile) to result in 25
mg of the title compound as a white solid. MS and H-NMR
were consistent with the proposed structure.

20

- 546 -

Example 291

Preparation of β -[[2-[[[3,5-bis[(aminoiminomethyl)amin]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzene-
propanoic acid, bis(trifluoroacetate) salt

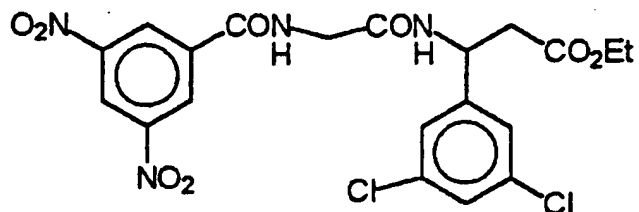
Step A

Glycine (20 g, 266 mmol) was added to water (200 mL), followed by addition of potassium hydroxide (20 g, 357 mmol) and cooled to 0°C in an ice bath. To this mixture 3,5-dinitrobenzoyl chloride (20 g, 108 mmol) was added in acetonitrile (20 mL) drop-wise over a 10 minute period. After complete reaction (3-4 hours) concentrated hydrochloric acid was added until pH=1. The product was filtered, washed with water and air dried (20 g). MS and H-NMR were consistent with the proposed structure.

- 547 -

Step B

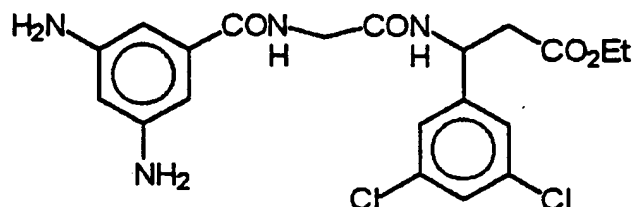
5



10 N,N'-disuccinimidyl carbonate (DSC) (1.2 g) was added to the compound produced in Step A (2 g) in dry dimethylformamide (10 mL) followed by addition of dimethylaminopyridine (200 mg). After a period of 20 minutes, DL ethyl 3-amino-3-(3,5 dichlorophenyl) propionate hydrochloride (1.2 g) was added followed by addition of NMM (2.0 mL). After complete reaction
15 (4 hours) the product was isolated by extraction into ethyl acetate and dried over Na₂SO₄ to result in an yellow oil (2.1 g). MS and H-NMR were consistent with the proposed structure.

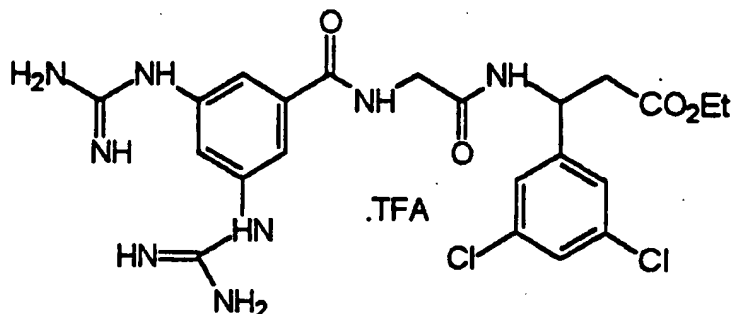
20 Step C

25



The compound produced in Step B was subjected to the conditions discribed in Tetrahedron Letters, Vol. 25,
30 1984, 839-842 to reduce of the nitro group. The reduction was performed on 2.5 g of nitro compound to give 2.1 g of the 3,5-dianilino derivative. MS and H-NMR were consistent with the proposed structure.

- 548 -

Step D

10 The compound produced in Step C was guanidated
according to the method in Example M on a 2 g scale (using
4 g of the guanidating agent) and purified by reverse
phase chromatography (water/acetonitrile) to result in
800 mg of a white solid. MS and H-NMR were consistent
15 with the proposed structure.

Step E

20 The compound produced in Step D (500 mg) was
dissolved in water/acetonitrile (1:1), followed by
addition of lithium hydroxide (100 mg). The reaction was
allowed to stir at 25°C, and monitored by HPLC. After
complete hydrolysis (1-2 hours) trifluoroacetic acid was
added until pH = 2. The product was purified by reverse
phase chromatography (water/acetonitrile) to result in
25 450 mg of the title compound as a white solid. MS and
H-NMR were consistent with the proposed structure.

- 549 -

Example 292

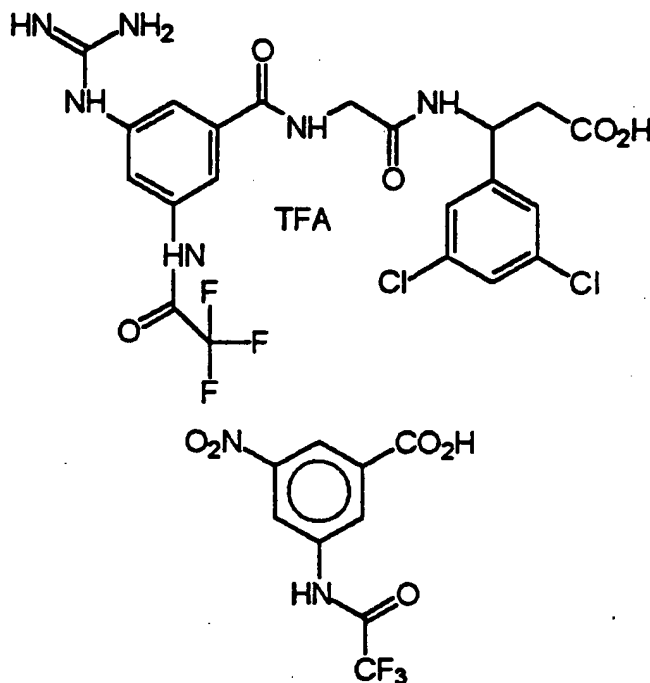
Preparation of β -[[2-[[[3-[(amin iminomethyl)amino]-5-(trifluoroacetyl)amino]phenyl]carbonyl]amino]acetyl]-amino]-3,5-dichlorobenzenepropanoic acid, trifluoroacetate salt

5

10

15

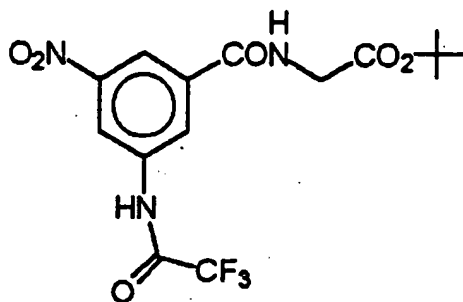
20

Step A

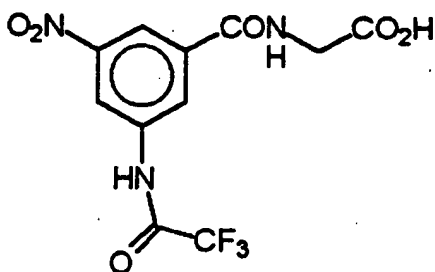
A mixture of 5-amino-3-nitro benzoic acid (Lancaster) (3 g) and trifluoroacetic anhydride (Sigma) (20 mL) in methylene chloride was stirred for 2 days at 25°C. The solvent was removed under reduced pressure to leave an oil. To the oil was added water (50 mL) and the product filtered (4.5 g). The product was dried in an oven at 70°C for 16 hours. MS and H-NMR were consistent with the proposed structure.

30

- 550 -

Step B

5
10 N,N'-disuccinimidyl carbonate (DSC) (3 g) was added to the compound produced in Step A (2.7 g) in dry dimethylformamide (4 mL) followed by addition of dimethylaminopyridine (200 mg). After a period of 20 minutes, tert-butyl glycine hydrochloride (2.7 g) was
15 added followed by addition of NMM (2.0 mL). After complete reaction (4 hours) the product was isolated by extraction into ethyl acetate and dried over Na₂SO₄ to result in an yellow oil (3.3 g). MS and H-NMR were
20 consistent with the proposed structure.

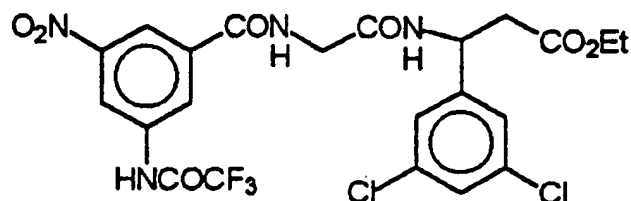
Step C

25
30 The compound produced in Step B (3 g) was dissolved in methylene chloride (50 mL). To this mixture TFA (20 mL) was added. The mixture was stirred for 12 hours. The solvent was removed under reduced pressure followed by addition of ether. The solid (2.7 g) was filtered and

- 551 -

dried in a vacuum oven for 1-2 hours. MS and H-NMR were consistent with the proposed structure.

Step D

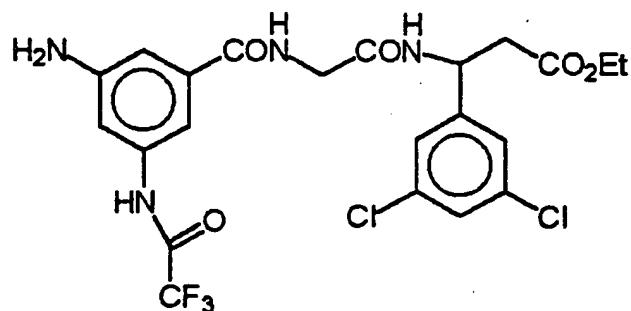


10

N,N'-disuccinimidyl carbonate (DSC) (1.5 g) was added to the product of Step C (1.2 g) in dry dimethylformamide (10 mL) followed by addition of dimethylaminopyridine (200 mg). After a period of 20 minutes DL ethyl 3-amino-3-(3,5 dichlorophenyl) propionate hydrochloride (1.7 g) was added followed by addition of NMM (2.0 mL). After complete reaction (4 hours) the product was isolated by extraction into ethyl acetate and dried over Na₂SO₄ to result in an yellow oil (2.1 g). MS and H-NMR were consistent with the proposed structure.

20

Step E



25

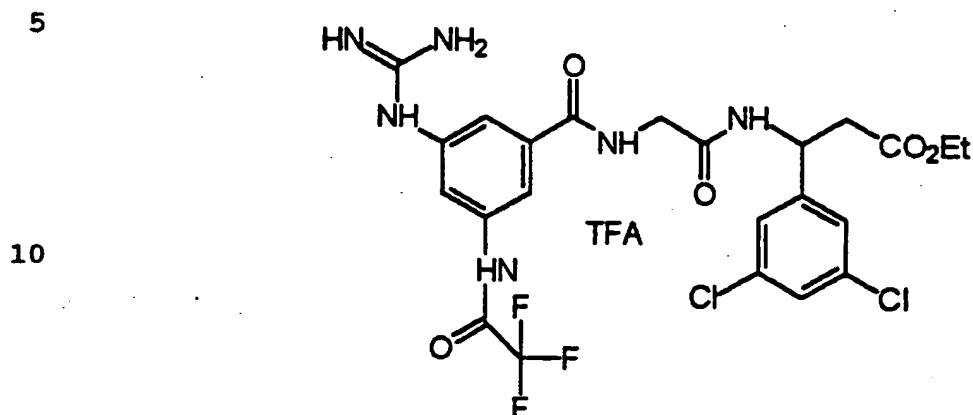
30

The compound produced in Step D was subjected to the conditions described in Tetrahedron Letters, Vol. 25, 1984, 839-842 to reduce the nitro group. The reduction was performed on 1.8 g of nitro compound to give 1.8 g of

- 552 -

the 3-anilino derivative. MS and H-NMR were consistent with the proposed structure.

Step F



15 The compound produced in Step E was guanidated according to the method in Example M on a 1.5 g scale (using 3 g of the guanidating agent) and purified by reverse phase chromatography (water/acetonitrile) to result in 750 mg of the above compound as a white solid.

20 MS and H-NMR were consistent with the proposed structure.

Step G

The compound produced in Step F (500 mg) was dissolved in water/acetonitrile (1:1), followed by the

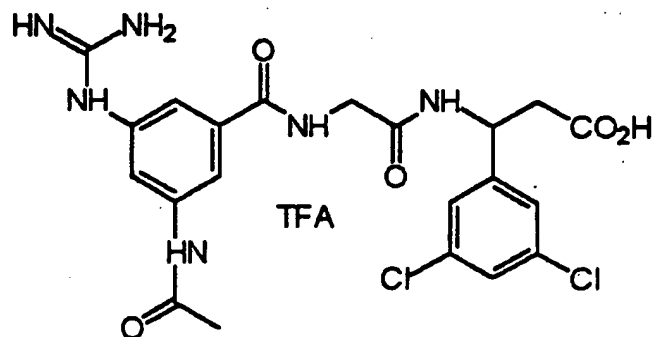
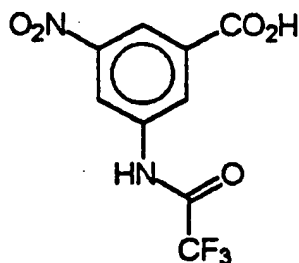
25 addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse

30 phase chromatography (water/acetonitrile) to result in 300 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

- 553 -

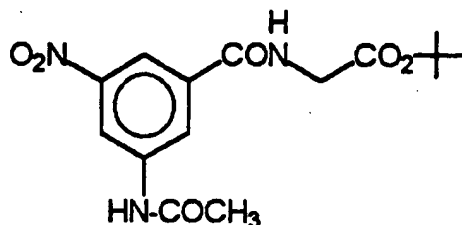
Example 293

Preparation of β -[[2-[[[3-(acetylamino)-5-
[(aminoiminomethyl)amino]phenyl]carbonyl]amino]-
acetyl]amino]-3,5-dichlorobenzenepropanoic
acid, trifluoroacetate salt

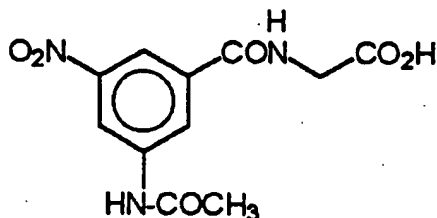
Step A

A mixture of 5-amino-3-nitro benzoic acid (Lancaster)
(5 g) and acetic anhydride (Sigma) (10 mL) in methylene
chloride was stirred for 2 days at 25°C. The solvent was
removed under reduced pressure to leave an oil. To the
oil was added water (50 mL) and the product filtered
(4.5 g). The product was dried in an oven at 70°C for 16
hours. MS and H-NMR were consistent with the proposed
structure.

- 554 -

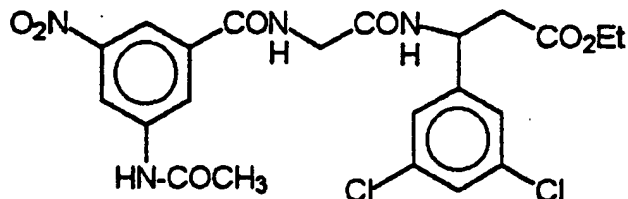
Step B

5
10 N,N'-disuccinimidyl carbonate (DSC) (3 g) was added to the compound produced in Step A (3 g) in dry dimethylformamide (6 mL) followed by addition of dimethylaminopyridine (200 mg). After a period of 20 minutes tert-butyl glycine hydrochloride (2.1 g) was added followed by addition of NMM (2.0 mL). After complete
15 reaction (4 hours) the product was isolated by extraction into ethyl acetate and dried over Na₂SO₄ to result in a yellow oil (3.3 g). MS and H-NMR were consistent with the proposed structure.

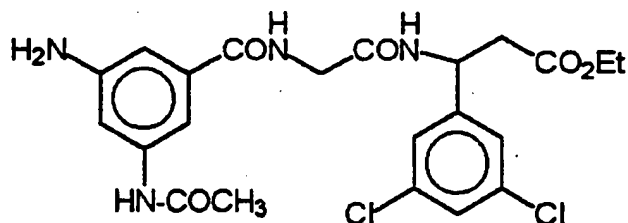
20 Step C

25
30 The compound produced in Step B (3 g) was dissolved in methylene chloride (10 mL). To this mixture TFA (10 mL) was added. The mixture was stirred for 12 hours. The solvent was removed under reduced pressure followed by addition of addition of ether. The solid (3 g) was filtered and dried in a vacuum oven for 1-2 hours. MS and H-NMR were consistent with the proposed structure.

- 555 -

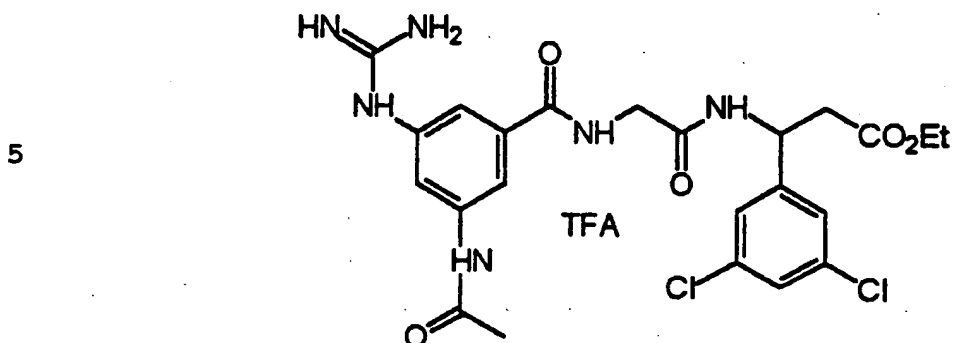
Step D

5
10
15
20
25
N,N'-disuccinimidyl carbonate (DSC) (1.5 g) was added to the product from Step C (1.2 g) in dry dimethylformamide (10 mL) followed by addition of dimethylaminopyridine (200 mg). After a period of 20 minutes DL ethyl 3-amino-3-(3,5 dichlorophenyl) propionate hydrochloride (1.7 g) was added followed by addition of NMM (2.0 mL). After complete reaction (4 hours) the product was isolated by extraction into ethyl acetate and dried over Na₂SO₄ to result in a tan solid (2 g). MS and H-NMR were consistent with the proposed structure.

Step E

20
25
30
The compound produced in Step D was subjected to the conditions described in Tetrahedron Letters, Vol. 25, 1984, 839-842 to reduce the nitro group. The reduction was performed on 1.5 g of nitro compound to give 1.5 g of the 3-anilino derivative. MS and H-NMR were consistent with the proposed structure.

- 556 -

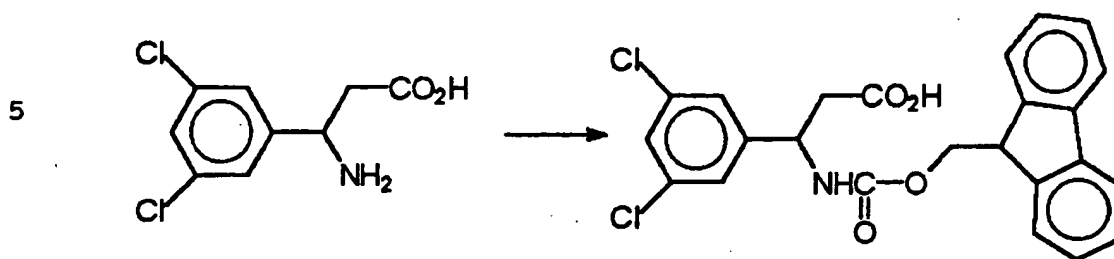
Step F

The compound produced in Step E was guanidated according to the method in Example M on a 1.4 g scale (using 2 g of the guanidating agent) and purified by reverse phase chromatography (water/acetonitrile) to result in 750 mg of the above compound as a white solid. MS and H-NMR were consistent with the proposed structure.

Step G

The compound produced in Step F (300 mg) was dissolved in water/acetonitrile (1:1), followed by the addition of lithium hydroxide (100 mg). The reaction was allowed to stir at 25°C, and monitored by HPLC. After complete hydrolysis (1-2 hours) trifluoroacetic acid was added until pH = 2. The product was purified by reverse phase chromatography (water/acetonitrile) to result in 200 mg of the title compound as a white solid. MS and H-NMR were consistent with the proposed structure.

- 557 -

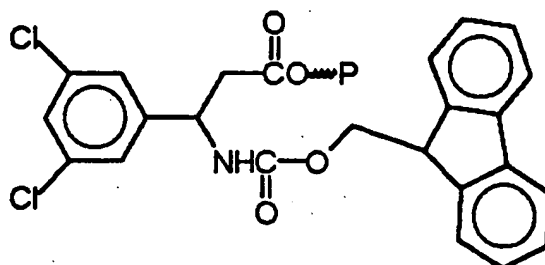
Examples 294-296Step A

To a 2L-3-neck round bottom flask equipped with
10 mechanical stirrer was added β -amino-3,5-dichloro-
benzenepropanoic acid (52.78 g, 0.2255 mol). The β -amino-
3,5-dichlorobenzenepropanoic acid was dissolved in 900 mL
of acetone and 300 mL of water and sodium carbonate was
added (3.0 eq., 71.70 g, 0.6765 mol). The pH = 10. The
15 Fmoc succinimidyl carbonate (Sigma Chemical Co., 1.0 eq.,
76.06 g, 0.2255 mol) was dissolved in 600 mL of acetone
and added slowly to the basic aqueous solution via
addition funnel over 45 minutes. The reaction was stirred
for 16 hours at room temperature. HPLC analysis (Waters,
20 C18, reverse phase, 25 cm column, 50-90% acetonitrile in
water over 30 minutes) indicated that the β -amino-3,5-
dichlorobenzenepropanoic acid was consumed. The acetone
was removed from the reaction mixture *in vacuo*. The basic
aqueous phase was acidified to pH = 3 using 3.0 N
25 hydrochloric acid. In a 2L separatory funnel the acid
layer was washed with 1L of ethyl acetate, the water layer
was removed and the organic layer was washed (2 x 250 mL
water, 2 x 250 mL saturated sodium chloride). The organic
layer was dried (magnesium sulfate), filtered and
30 concentrated *in vacuo* to 300 mL. Petroleum ether was
added (300 mL) and a white flocculent solid precipitated.
After 24 hours of air drying, isolated 38.49 g as a first
crop (38% yield). The mother liquor was saved for future
use. NMR (DMSO): 2.62-2.72 (m, 2H), 4.15-4.32 (m, 1H),
35 7.21-7.40 (m, 5H), 7.45 (s, 1H), 7.60-7.70 (m, 2H), 7.85

- 558 -

(d, $j=7$ Hz, 2H), 7.99 (d, $j=7$ Hz, 1H). MS (FAB) m/e (relative intensity): 456.2 (20), 179 (100).

Step B

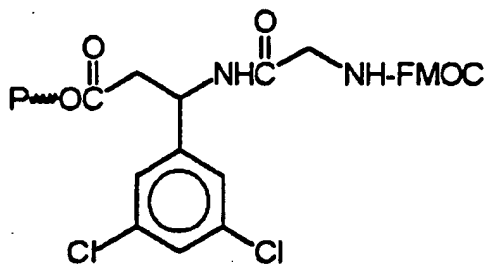


Wang resin (25.0 g, 28.0 mmol) was placed in a 1L 3-neck round bottom flask fitted with an overhead stirrer and nitrogen inlet. The resin was swelled with 250 mL of methylene chloride for 15 minutes then drained. The Fmoc protected amino acid produced in Step A (25.66 g, 56.0 mmol) was activated in a separate 500 mL round bottom flask by dissolving in methylene chloride/dimethylformamide (4:1, 125 mL) and adding diisopropylcarbodiimide (DIC, 8.77 mL, 56.0 mmol) via syringe, followed by addition of dimethylaminopyridine (DMAP, 0.342 g, 2.8 mmol). The solution was stirred at 25°C for 15 minutes, then added to the preswelled Wang resin. The slurry was stirred for 2 hours at 25°C. The reaction was drained and washed with methanol (3 x 250 mL), methylene chloride (3 x 250 mL) and diethyl ether (3 x 250 mL). The resin was then swelled in 250 mL of methylene chloride and drained. The activated product of Step A (12.83 g, 28.0 mmol, DIC, 4.36 mL, 28.0 mmol, DMAP, 0.170 g, 1.4 mmol in 100 mL methylene chloride/dimethylformamide 4:1) was added to the swelled resin. The slurry was stirred at 25°C for 1 hour. The resin was drained and washed as before. Elemental analysis calculated for resin bound material:

Calculated: C, 81.31; H, 6.30; N, 1.05; Cl, 5.33.

Found: C, 79.03; H, 6.37; N, 1.16; Cl, 5.74.

- 559 -

Step C

5

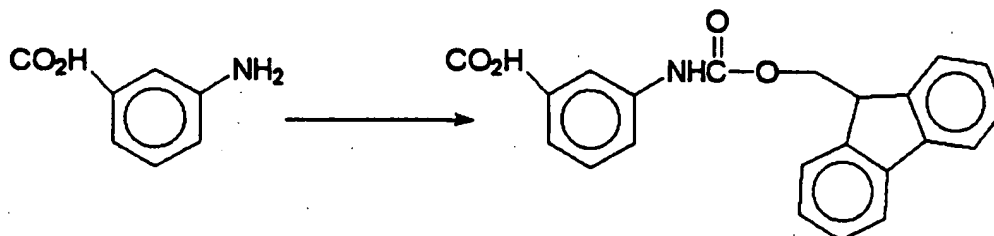
10 The product of Step B (28.0 mmol) was preswelled in a 1L 3-neck round bottom flask equipped with overhead stirrer and nitrogen inlet using 250 mL of methylene chloride for 15 minutes. The solvent was drained and a 20% piperidine/dimethylformamide solution (125 mL) was added and the slurry was stirred at 25°C for 2 hours. The resin was drained and washed with dimethylformamide (3 x 100 mL), methanol (3 x 100 mL) methylene chloride (3 x 100 mL) and diethyl ether (3 x 100 mL). The resin was dried using house vacuum for 1 hour. An activated solution of FMOC-Glycine (20.81 g, 70.0 mmol, DIC, 10.95 mL, 70.0 mmol, DMAP, 0.85 g, 7.0 mmol. In 150 mL methylene chloride/dimethylformamide, 4:1) was added to the preswelled resin via syringe and stirred at 25°C for 2 hours. The resin was drained and washed (methylene chloride, methanol and diethyl ether, each 3 x 100 mL).

25 The resin was preswelled with 250 mL of methylene chloride for 15 minutes, drained and a solution of activated FMOC-Glycine (10.45 g, 35.0 mmol, DIC, 5.42 mL, 35.0 mmol, DMAP, 0.42 g, 3.5 mmol in 100 mL methylene chloride/dimethyl formamide 4:1) was added to the swelled resin via syringe. The slurry was stirred at 25°C for 1 hour. The resin was drained and washed (methylene chloride, methanol, diethyl ether, 3 x 100 mL each). The resin was vacuum dried for 1 hour. The Kaiser test (Kaiser, E., Color Test for D tection of Free Terminal

30

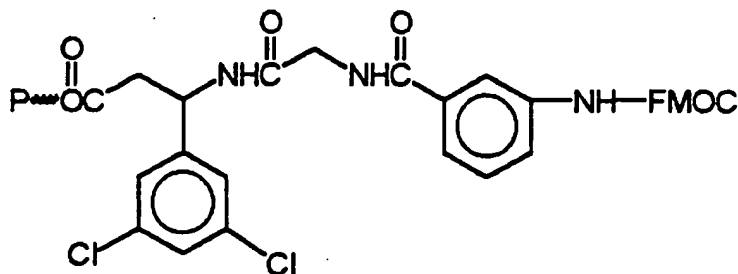
- 560 -

Amino Groups in the Solid-Phase Synthesis of Peptides. Anal. Biochem. 1970, 34, 595-598) indicated coupling was complete.

5 Step D

In a 500 mL bottom flask equipped with magnetic stirrer, 3-amino-benzoic acid (Aldrich, 10.0 g, 50.8 mmol) was dissolved in 50 mL of dioxane and 133 mL of 10% sodium carbonate. The stirred solution was cooled to 0°C (ice/water) and a solution of fluorenylmethyl chloroformate (13.78 g, 53.3 mmol, in 50 mL dioxane) was added dropwise over 15 minutes. The reaction was warmed to 25°C overnight. HPLC analysis (as described earlier) indicated that the starting material was consumed. 500 mL of water was added to the reaction mixture and a white precipitate formed immediately. The solid was collected, washed with 10% citric acid and dried under vacuum. Isolated 15.23 g, (83.4% yield) of a white flocculent solid. NMR (DMSO): 4.18-4.25 (m, 3H), 7.25-7.41 (m, 6H), 7.62-7.72 (m, 3H), 7.89-7.90 (m, 3H). MS(FAB): product ion $\text{M}+\text{H}$ observed at m/z 360.

- 561 -

Step E

20.0 g of the product of Step C (22.4 mmol) was preswelled in 500 mL of methylene chloride for 30 minutes. The solvent was drained and 250 mL of 20% piperidine/dimethyl formamide was added and allowed to stir at 25°C for 40 minutes. The resin was drained and washed with dimethyl formamide, methanol, methylene chloride, and diethyl ether (each solvent, 3 x 150 mL). The Kaiser test indicated the deprotection was complete. The resin was dried using house vacuum for 45 minutes. The resin was then preswelled using 250 mL of methylene chloride, drained and the activated product of Step D (13.54 g, 35.5 mmol, DIC, 5.55 mL, 35.5 mmol, DMAP, 0.88 g, 7.2 mmol, in 100 mL methylene chloride/dimethyl formamide 4:1) was added to the preswelled resin. The reaction was stirred for 16 hours at 25°C. The resin was drained and washed as previously described. The Kaiser test indicated that the reaction was not complete. The coupling reaction was repeated, the resin was drained and washed. A repeat Kaiser test indicated that the coupling reaction was complete. A small portion of the resin was Fmoc deprotected (30 minutes with 20% piperidine/dimethyl formamide) then cleaved off resin (1 hour with 95% trifluoroacetic acid/water) for NMR analysis. NMR (DMSO): 2.68-2.78 (m, 2H), 3.88 (d, $j=7$ Hz, 2H), 5.06-5.20 (m, 1H), 7.32-7.69 (m, 4H), 7.54 (t, $j=8$ Hz, 1H), 7.76

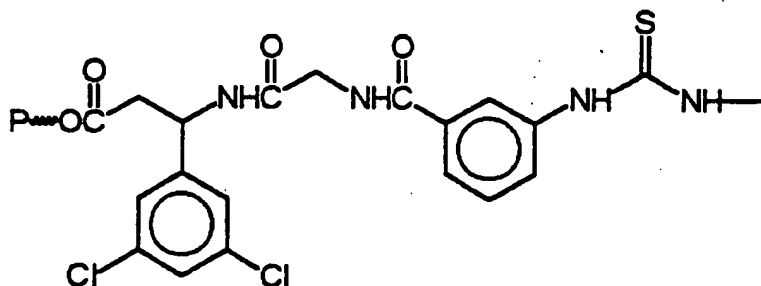
- 562 -

(s, 1H), 7.83 (d, $j=8$ Hz, 1H), 8.57 (d, $j=9$ Hz, 1H), 8.87 (t, $j=9$ Hz, 1H).

Step F

5

10



15

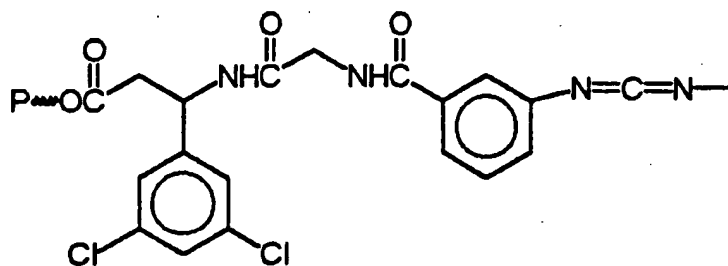
20

25

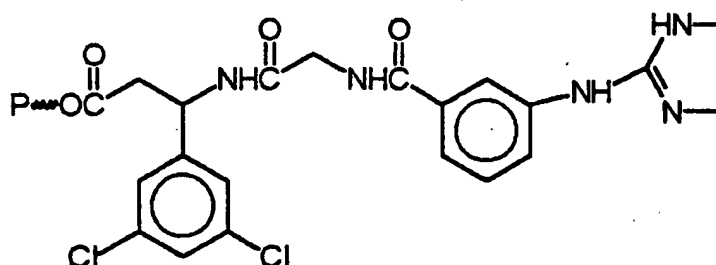
30

The resin of Step E (2.0 g, 2.0 mmol) in a 100 mL round bottom flask, was preswelled with 20 mL of dimethyl formamide, drained, then treated with 20 mL of 20% piperidine/dimethyl formamide for 40 minutes at 25°C. The resin was filtered and washed with dimethyl formamide, methanol, methylene chloride and diethyl ether (3 x 10 mL, each). The Kaiser test was inconclusive, and the deprotection step and washings were repeated. The repeat Kaiser test was still inconclusive, and the material used as is. The 2.0 g of resin was split into two 1.0 g portions and placed into 2 dram glass vials. Dimethyl formamide (4.0 mL/vial) was added, followed by methyl isothiocyanate (1.4622 g, 20 mmol). The vials were tightly capped and heated to 80°C for 4 hours. The resin was filtered and washed with dimethyl formamide, methanol, methylene chloride, and diethyl ether (3 x 10 mL, each). The resin was dried *in vacuo*.

- 563 -

Step G

The resin product from Step F was transferred to a
fritted, 100 mL reaction vessel. The resin was swelled
with methylene chloride (3 x 10 mL) and drained. In a
separate vial 2-chloro-1-methylpyridiniumiodide (Aldrich,
0.405 g, 1.58 mmol) was dissolved in 5 mL of
dimethylformamide/methylene chloride 4:1 and added to the
preswelled resin, followed by triethylamine (0.441 mL,
3.17 mmol). The reaction slurry was stirred for 8 hours
at 25°C. The resin was drained, and washed with
dimethylformamide and methylene chloride (3 x 10 mL
each). The resin was dried in vacuo.

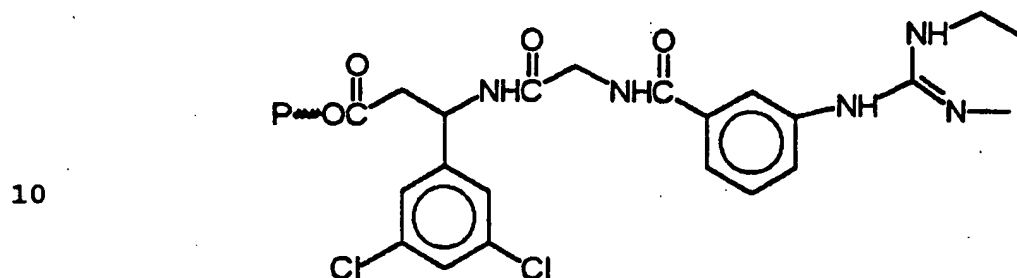
Step H

The resin product from Step G (0.666 g, 0.7 mmol) was
transferred to a 15 mL fritted vessel and suspended in 3.5
mL of dimethylformamide/methylene chloride (1:1).
Methylamine (2.0 M in tetrahydrofuran, 4.4 mL, 8.8 mmol)
was added to the resin slurry and allowed to stir at 25°C
for 16 hours. The resin was drained, and washed with

- 564 -

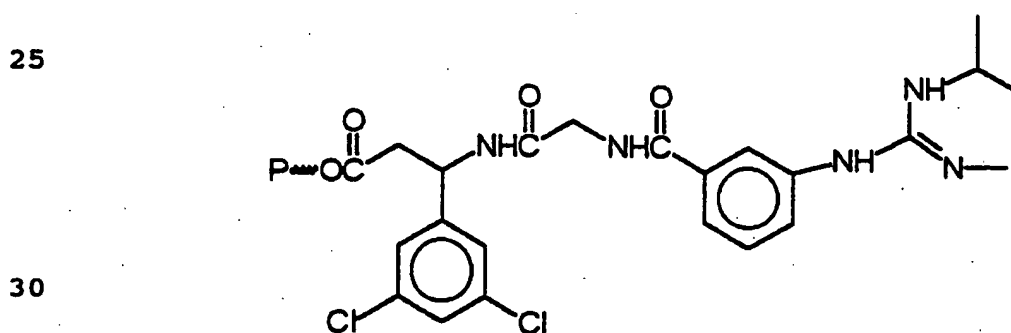
dimethylformamide, methanol, methylene chloride and diethyl ether (3 x 10 mL each). The resin was dried in vacuo for 1 hour.

5 Step I



15 The resin product from Step G (0.666 g, 0.7 mmol) was transferred to a 15 mL fritted vessel and suspended in 3.5 mL dimethylformamide/methylene chloride (1:1). Ethylamine (2.0 M in tetrahydrofuran, 4.4 mL, 8.8 mmol) was added to the resin slurry and allowed to stir at 25°C for 16 hours. The resin was drained, and washed with dimethylformamide, 20 methanol, methylene chloride and diethyl ether (3 x 10 mL each). The resin was dried in vacuo for 1 hour.

Step J



- 565 -

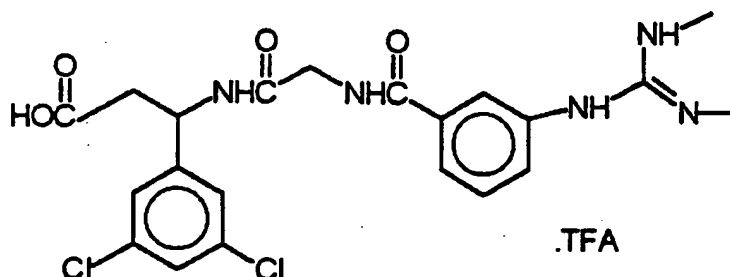
The resin product from Step G (0.666 g, 0.7 mmol) was transferred to a 15 mL fritted vessel and suspended in 3.5 mL dimethylformamid /methylene chloride (1:1).

- 5 Isopropylamine (0.749 mL, 8.8 mmol) was added to the resin slurry and allowed to stir at 25°C for 16 hours. The resin was drained, and washed with dimethylformamide, methanol, methylene chloride and diethyl ether (3 x 10 mL each). The resin was dried in vacuo for 1 hour.

- 566 -

Example 294

Preparation of (±) 3,5-dichloro-β-[[2-[[[3-
5 [[(methylamino) (methylimino) methyl] amino]-
phenyl] carbonyl] amino] acetyl] amino]-
benzenepropanoic acid,
trifluoroacetate salt

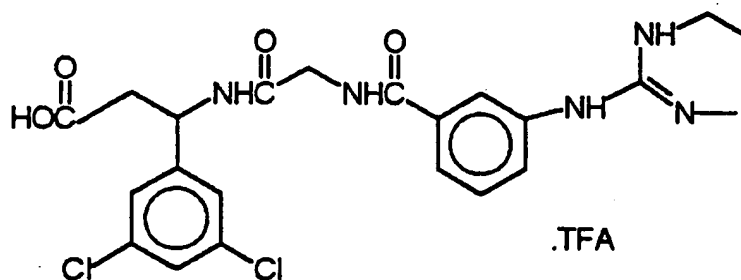


The resin product from Step H was treated with 2.5 mL of 95% trifluoroacetic acid/water for 1 hour at 25°C. The filtrate was collected. The resin was washed with 2 x 1 mL of 50% trifluoroacetic acid/methylene chloride and the filtrate collected. The resin was washed once more with 1 mL of methylene chloride. All filtrates were combined into a tared 2 dram vial and concentrated under nitrogen flow. Toluene (1 mL) was added to aid in removing excess trifluoroacetic acid, and the sample was concentrated again under nitrogen. Lastly methylene chloride (1 mL) was added and the sample was reconcentrated to give 198.3 mg of a golden oil. HPLC (as described earlier, 220 nm) shows a 91% pure major peak. NMR (DMSO): 2.72 (d, j=7Hz, 2H), 2.79 (s, 6H), 3.87 (d, j=7 Hz, 2H), 5.11-5.20 (m, 1H), 7.30-7.58 (m, 5H), 7.70-7.80 (m, 4H), 8.55 (d, j=8 Hz, 1H), 8.76 (t, j=3Hz, 1H), 9.39 (s, 1H). MS(ES): product ion observed at m/z 480.

- 567 -

Example 295

Preparation of (±) 3,5-dichloro-β-[[2-[[[3-
[[(ethylamino) (methylimino) methyl] amino]-
phenyl] carbonyl] amino] acetyl] amino]-
benzenepropanoic acid,
trifluoroacetate salt

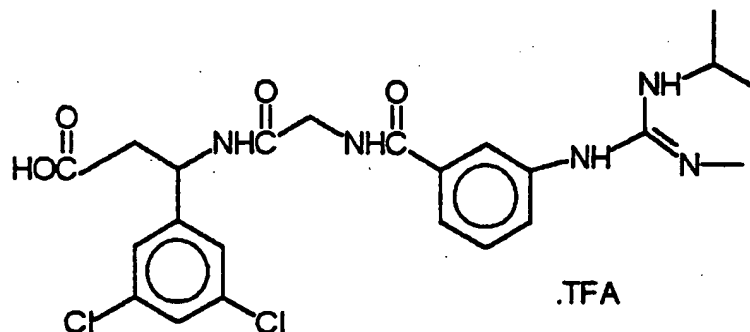


The resin product from Step I was treated with 2.5 mL of 95% trifluoroacetic acid/water for 1 hour at 25°C. The filtrate was collected. The resin was washed with 2 x 1 mL of 50% trifluoroacetic acid/methylene chloride and the filtrate collected. The resin was washed once more with 1 mL of methylene chloride. All filtrates were combined into a tared 2 dram vial and concentrated under nitrogen flow. Toluene (1 mL) was added to aid in removing excess trifluoroacetic acid, and the sample was concentrated again under nitrogen. Lastly methylene chloride (1 mL) was added and the sample was reconcentrated to give 261.2 mg of a golden oil. HPLC (as described earlier, 220 nM) shows a 94% pure major peak. NMR (DMSO): 1.11 (t, j=7Hz, 3H), 2.72 (d, J=7 hZ, 2H), 2.79 (s, 3H), 3.25-3.60 (m, 2H), 3.87 (d, j=7 Hz, 2H), 5.02-5.20 (m, 1H), 7.30-7.58 (m, 5H), 7.70-7.85 (m, 4H), 8.55 (d, j=8 Hz, 1H), 8.76 (t, j=3Hz, 1H), 9.40 (s, 1H). MS(ES): product ion observed at m/z 494.

- 568 -

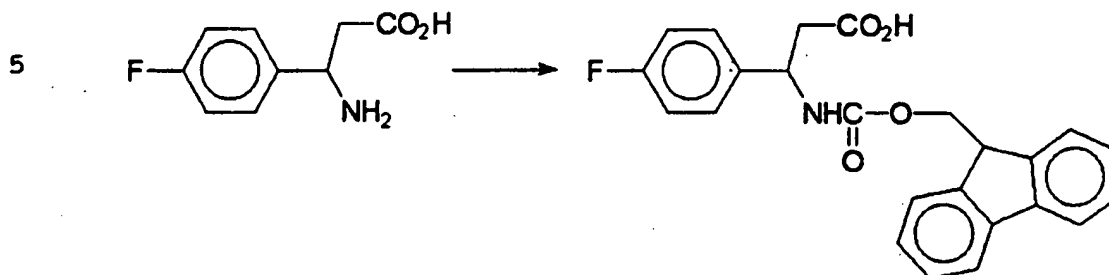
Example 296

Preparation of (±) 3,5-dichloro-β-[[2-[[[3-[[[(1-methylethyl)amino](methylimino)methyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid, trifluoroacetate salt



The resin product from Step J was treated with 2.5 mL of 95% trifluoroacetic acid/water for 1 hour at 25°C. The filtrate was collected. The resin was washed with 2 x 1 mL of 50% trifluoroacetic acid/methylene chloride and the filtrate collected. The resin was washed once more with 1 mL of methylene chloride. All filtrates were combined into a tared 2 dram vial and concentrated under nitrogen flow. Toluene (1 mL) was added to aid in removing excess trifluoroacetic acid, and the sample was concentrated again under nitrogen. Lastly methylene chloride (1 mL) was added and the sample was reconcentrated to give 330.3 mg of a golden oil. HPLC (as described earlier, 220 nM) shows an 89% pure major peak. NMR (DMSO): 1.15 (d, j=7Hz, 6H), 2.72 (d, j=7Hz, 2H), 2.79 (d, j=7 Hz, 3H), 3.79-3.92 (m, 3H), 5.05-5.20 (m, 1H), 7.30-7.50 (m, 5H), 7.60-7.78 (m, 4H), 8.55 (d, j=8 Hz, 1H), 8.76 (t, j=3Hz, 1H), 9.40 (s, 1H). MS(ES): product ion observed at m/z 508.

- 569 -

Examples 297-299Step A

10 To a 50 mL round bottom flask equipped with magnetic stirrer was added 3-amino-3-(4-fluoro-phenyl)-propionic acid, (0.300 g, 1.64 mmol). The propionic acid was dissolved in 1 mL of acetone and 6 mL of water and sodium carbonate was added (0.53 g, 4.92 mmol). The pH=10. The

15 FMOC succinimidyl carbonate (Sigma Chemical Co., 0.553 g, 1.64 mmol) was dissolved in 6 mL of acetone and added slowly to the basic aqueous solution via addition funnel over 20 minutes. The reaction was stirred for 16 hours at room temperature. HPLC analysis (Waters, C18, reverse

20 phase, 25 cm column, 50-90% acetonitrile in water over 30 minutes) indicated that the starting material was consumed. The acetone was removed from the reaction mixture *in vacuo*. The basic aqueous phase was acidified to pH=3 using 3.0 N hydrochloric acid. In a 50 mL

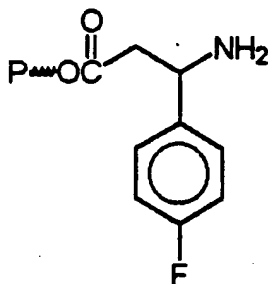
25 separatory funnel the acid layer was washed with 15 mL of ethyl acetate, the water layer was removed and the organic layer was washed (2 x 30 mL water, 2 x 30 mL saturated sodium chloride). The organic layer was dried (magnesium sulfate), filtered and concentrated *in vacuo*. Petroleum

30 ether was added (10 mL) and a white flocculent solid precipitated. After 24 hours of air drying, isolated 0.582 g as a first crop (87.5% yield). The mother liquor was saved for future use. NMR (DMSO): 2.55-2.75 (m, 2H), 4.10-4.30 (m, 3H), 4.85-4.95 (m, 1H), 7.12 (t, *j*=8 Hz,

- 570 -

2H), 7.24-7.42 (m, 5H), 7.64 (d, $j=8$ Hz, 2H), 7.82-7.94 (m, 3H). MS (FAB): product ion $M+Li$ observed at m/z 412.

Step B

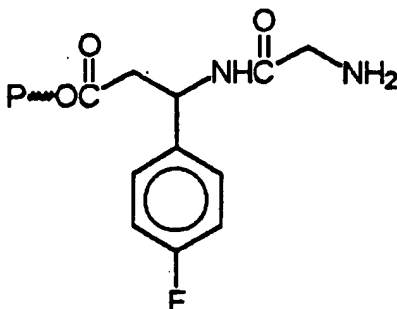


Wang resin (0.60 g, 0.36 mmol) was placed in a 100 mL round bottom flask. The resin was swelled with 8 mL of methylene chloride for 15 minutes then drained. The Fmoc protected amino acid of Step A (0.365 g, 0.9 mmol) was activated in a separate 25 mL round bottom flask by dissolving in methylene chloride/dimethylformamide (4:1, 19 mL) and adding diisopropylcarbodiimide (DIC, 0.141 mL, 0.90 mmol) via syringe, followed by the addition of dimethylaminopyridine (DMAP, 22 mg, 0.18 mmol). The solution was stirred at 25°C for 15 minutes, then added to the preswelled Wang resin. The slurry was stirred for 2 hours at 25°C. The reaction was drained and washed with methanol (3 x 10 mL), methylene chloride (3 x 10 mL) and diethyl ether (3 x 10 mL). To ensure complete reaction, the coupling sequence was repeated. After drying *in vacuo* the resin was swelled with 8 mL of methylene chloride, drained and 8 mL of 20% piperidine/dimethylformamide was added and the slurry was stirred for 30 minutes. The resin was drained and washed as described previously. The resin was dried *in vacuo* for 1 hour. Elemental analysis calculated for resin bound material:

Calculated: C, 88.23; H, 7.36; N, 0.76; F, 1.03.

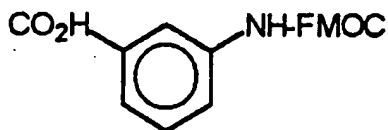
Found: C, 87.13; H, 7.31; N, 0.79; F, 1.06.

- 571 -

Step C

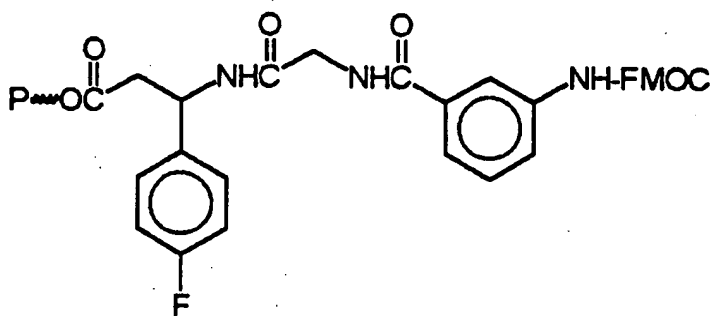
The resin product from Step B was swelled with 8 mL of methylene chloride, then drained. An activated solution of Fmoc-Glycine (0.267 g, 0.90 mmol, DIC, 0.140 mL, 0.90 mmol, DMAP, 22 mg, 0.18 mmol. In 10 mL methylene chloride/dimethylformamide, 4:1) was added to the preswelled resin via syringe and stirred at 25°C for 2 hours. The resin was drained and washed (methylene chloride, methanol and diethyl ether, each 3 x 10 mL). The resin was preswelled with 20 mL of methylene chloride for 15 minutes, drained and the coupling reaction was repeated to ensure complete reaction. The Kaiser test (Kaiser, E., Color Test for Detection of Free Terminal Amino Groups in the Solid-Phase Synthesis of Peptides. Anal. Biochem. 1970, 34, 595-598) indicated the coupling was complete. The resin was then suspended in 8 mL of 20% piperidine/dimethylformamide for 30 minutes, drained and washed with dimethylformamide, methanol, methylene chloride, and diethyl ether (3 x 10 mL, each). The resin was dried *in vacuo* for 1 hour.

- 572 -

Step D

5

In a 500 mL round bottom flask equipped with magnetic stirrer, 3-amino-benzoic acid (Aldrich, 10.0 g, 50.8 mmol) was dissolved in 50 mL of dioxane and 133 mL of 10% sodium carbonate. The stirred solution was cooled to 0°C (ice/water) and a solution of fluorenylmethyl chloroformate (13.78 g, 53.3 mmol, in 50 mL dioxane) was added dropwise over 15 minutes. The reaction warmed to 25°C overnight. HPLC analysis (as described earlier) indicated that the starting material was consumed. 500 mL of water was added to the reaction mixture and a white precipitate formed immediately. The solid was collected, washed with 10% citric acid and dried under vacuum. Isolated 15.23 g, (83.4% yield) of a white flocculent solid. NMR (DMSO): 4.18-4.25 (m, 3H), 7.25-7.41 (m, 6H), 7.62-7.72 (m, 3H), 7.80-7.90 (m, 3H). MS (FAB): product ion M+H observed at m/z 360.

Step E

25

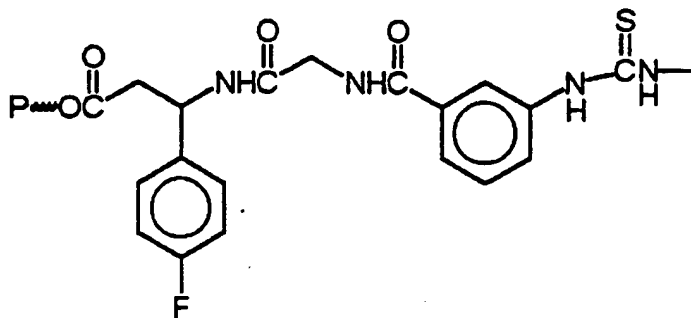
30

The resin product from Step C was then preswelled using 10 mL of methylene chloride, drained and the activated product of Step D (0.343 g, 0.90 mmol, DIC,

- 573 -

0.141 mL, 0.90 mmol, DMAP, 22 mg, 0.18 mmol, in 5 mL methylene chloride/dimethylformamid 4:1) was added to the preswelled resin. The reaction was stirred for 16 hours at 25°C. The resin was drained and washed as previously described. The Kaiser test indicated that the reaction was not complete. The coupling reaction was repeated, the resin was drained and washed. A repeat Kaiser test indicated that the coupling reaction was complete. The resin was dried *in vacuo* for 1 hour.

Step F



The resin product from Step E was placed in a 100 mL round bottom flask, was preswelled with 10 mL of dimethylformamide, drained, then treated with 20 mL of 20% piperidine/dimethylformamide for 10 minutes at 25°C. The resin was drained and the procedure was repeated. The resin was filtered and washed with dimethylformamide, methanol, methylene chloride and diethyl ether (3 x 10 mL, each). The Kaiser test indicated that the deprotection step was complete. The resin was placed into a glass 2 dram vial with dimethylformamide (8.0 mL), followed by methyl isothiocyanate (0.526 g, 7.2 mmol). The vial was tightly capped and heated to 80°C for 4 hours. The resin was filtered and washed with dimethylformamide, methanol, methylene chloride, and diethyl ether (3 x 10 mL, each).

- 574 -

The resin was dried in vacuo. Elemental analysis calculated for resin bound material:

Calc'd: C, 83.56; H, 6.46; N, 2.19; F, 1.03; S, 1.35.

Found: C, 82.32; H, 6.67; N, 2.53; F, 1.02; S, 1.44.

5

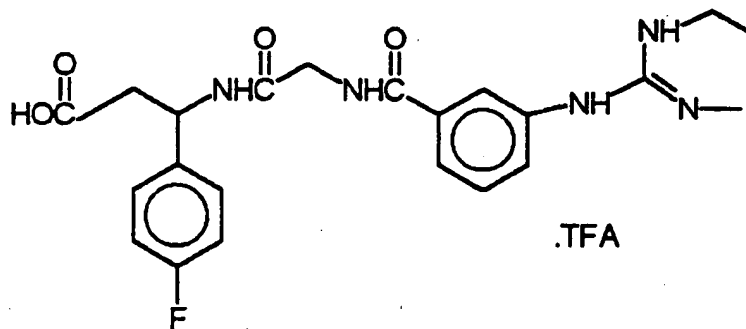
Step G

The resin product from Step F (100 mg, 0.06 mmol) was transferred to a 2 dram glass vial. The resin was swelled with methylene chloride (3 x 1 mL) and drained. In a separate vial 2-chloro-1-methylpyridiniumiodide (Aldrich, 18.4 mg, 0.072 mmol) was dissolved in 3 mL of dimethylformamide/methylene chloride 4:1 and added to the preswelled resin, followed by triethylamine (20.1 uL, 0.144 mmol). The reaction slurry was stirred for 16 hours at 25°C. The resin was drained, and washed with dimethylformamide, methanol, methylene chloride, and diethyl ether (3 x 4 mL, each). The resin was dried in vacuo for 3 hours. The resin was treated with 95% trifluoroacetic acid (1.5 mL) for 1 hour. The resin was filtered and washed with 50% trifluoroacetic acid/methylene chloride (2 x 1.0 mL) followed by methylene chloride (1 x 1.0 mL). The filtrates were combined and dried in vacuo in tared 2 dram glass vials.

- 575 -

Example 297

Preparation of (\pm) β -[[2-[[[3-[[[(ethylamino)-(methylimino)methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]-4-fluorobenzene-
propanoic acid, trifluoroacetate salt

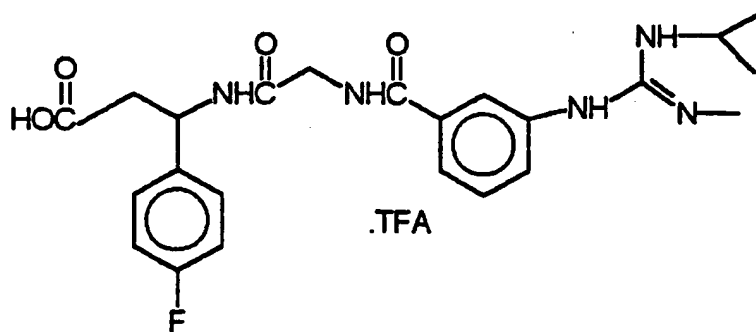


Isolated 28.1 mg of a golden oil. NMR (DMSO): 1.13 (t, $j=7$ Hz, 3H), 2.65-2.75 (m, 2H), 2.76-2.85 (m, 3H), 3.25 (t, $j=3$ Hz, 2H), 3.80-3.95 (m, 2H), 5.10-5.21 (m, 1H), 7.13 (t, $j=8$ Hz, 2H), 7.30-7.40 (m, 3H), 7.52 (t, $j=8$ Hz, 1H), 7.65-7.85 (m, 3H), 8.49 (d, $j=8$ Hz, 1H), 8.71 (t, $j=8$ Hz, 1H) 9.40 (s, 1H). HPLC (as described earlier, 220 nm) 90.15% pure. MS (ES): product ion observed at m/z 444.

- 576 -

Example 298

Preparation of (±) 4-fluoro-β-[[2-[[[3-[[[(1-
methylethyl)amino](methylimino)methyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoic acid,
trifluoroacetate salt

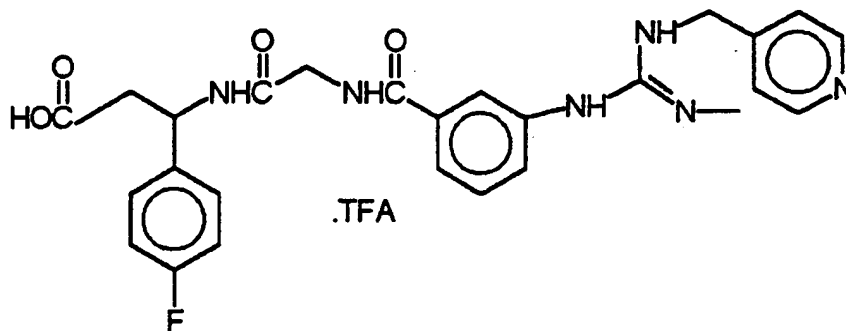


Isolated 44.9 mg of a golden oil. NMR (DMSO): 1.16
(d, j=7 Hz, 6H), 2.61-2.70 (m, 2H), 2.73-2.80 (m, 3H),
3.75-3.90 (m, 3H), 5.10-5.21 (m, 1H), 7.11 (t, j=8 Hz,
2H), 7.25-7.37 (m, 3H), 7.49 (t, j=8 Hz, 1H), 7.59-7.82
(m, 3H), 8.49 (d, j=8 Hz, 1H), 8.70 (t, j=3 Hz, 1H) 9.40
(s, 1H). HPLC (as described earlier, 220 nm) 98% pure.
MS (ES): product ion observed at m/z 458.

- 577 -

Example 299

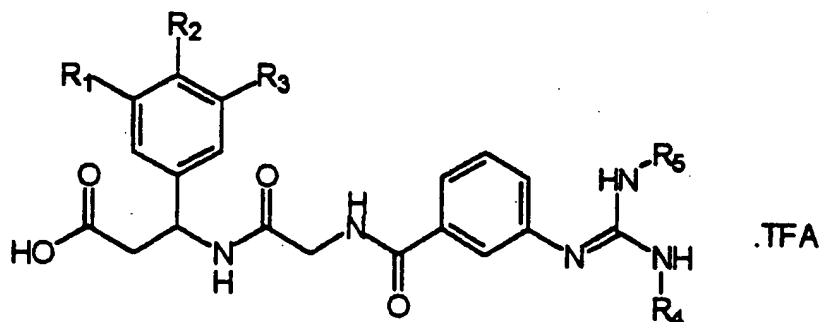
Preparation of (±) 4-fluoro-β-[[2-[[[3-[[[(4-pyridinylmethyl)amino](methylimino)methyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid, trifluoroacetate salt



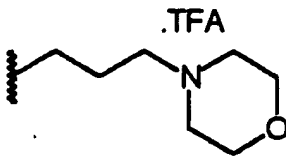
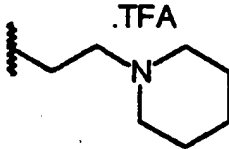
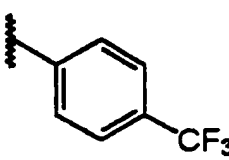
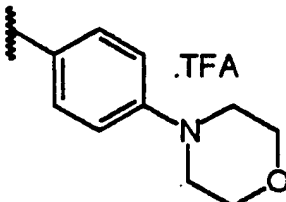
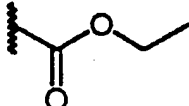
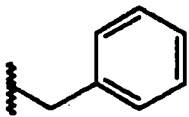

Isolated 31.6 mg of a golden oil. NMR (DMSO): 2.60-2.72 (m, 2H), 2.81-2.89 (d, $j=7$ Hz, 3H), 3.80-3.95 (m, 2H), 4.61-4.80 (bs, 2H), 5.10-5.21 (m, 1H), 7.01-7.22 (m, 4H), 7.29-7.44 (m, 3H), 7.50 (t, $j=8$ Hz, 1H), 7.65-7.85 (m, 3H), 8.40-8.50 (d, $j=8$ Hz, 1H), 8.70-8.85 (m, 3H), 9.73 (s, 1H). HPLC (as described earlier, 220 nm) 98% pure. MS(ES): product ion observed at m/z 507.

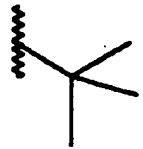
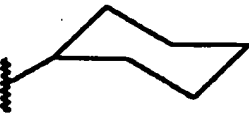
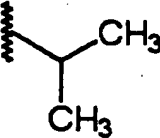
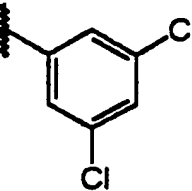
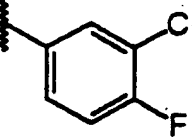
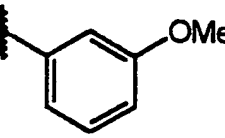
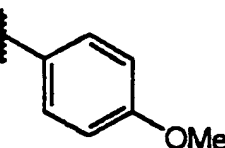
- 578 -

The following compounds are prepared according to analogous solid-phase synthetic methods described in Examples 294-299.

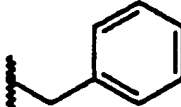
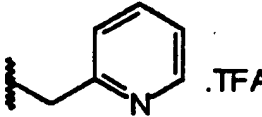
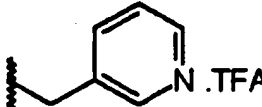
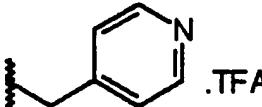
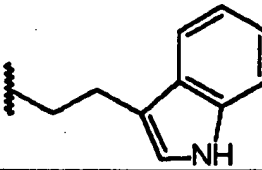
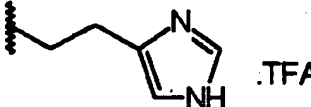
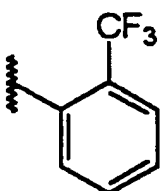


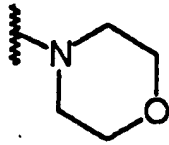
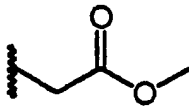
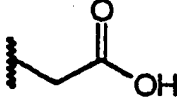
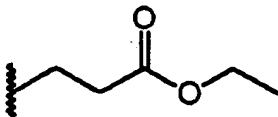
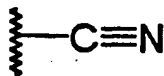
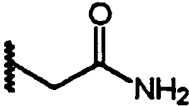
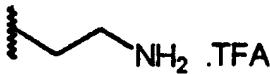

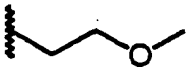
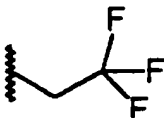
| Example | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ |
|---------|----------------|----------------|----------------|----------------|----------------|
| 300 | Cl | H | Cl | -H | |
| 301 | Cl | H | Cl | -H | |
| 302 | Cl | H | Cl | -H | |
| 303 | Cl | H | Cl | -H | |

| Example | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ |
|---------|----------------|----------------|----------------|----------------|--|
| 304 | Cl | H | Cl | -H |  |
| 305 | Cl | H | Cl | -H |  |
| 306 | Cl | H | Cl | -H | -CH ₂ CH ₃ |
| 307 | Cl | H | Cl | -H | -CH ₂ CH ₂ CH ₃ |
| 308 | Cl | H | Cl | -H |  |
| 309 | Cl | H | Cl | -H |  |
| 310 | Cl | H | Cl | -H |  |
| 311 | Cl | H | Cl | -H |  |
| 312 | Cl | H | Cl | -H |  |


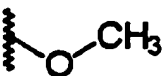
| Example | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ |
|---------|----------------|----------------|----------------|----------------|--|
| 313 | Cl | H | Cl | -H |  |
| 314 | Cl | H | Cl | -H |  |
| 315 | Cl | H | Cl | -H |  |
| 316 | Cl | H | Cl | -H |  |
| 317 | Cl | H | Cl | -H |  |
| 318 | Cl | H | Cl | -H |  |
| 319 | Cl | H | Cl | -H |  |

- 581 -

| Example | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ |
|---------|----------------|----------------|----------------|------------------|---|
| 320 | Cl | H | Cl | -CH ₃ |  |
| 321 | Cl | H | Cl | -CH ₃ |  .TFA |
| 322 | Cl | H | Cl | -CH ₃ |  .TFA |
| 323 | Cl | H | Cl | -CH ₃ |  .TFA |
| 324 | Cl | H | Cl | -CH ₃ |  |
| 325 | Cl | H | Cl | -CH ₃ |  .TFA |
| 326 | Cl | H | Cl | -CH ₃ | -CH ₂ (CF ₂) ₂ CF ₃ |
| 327 | Cl | H | Cl | -CH ₃ |  |

| Example | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ |
|---------|----------------|----------------|----------------|------------------|---|
| 328 | Cl | H | Cl | -CH ₃ |  |
| 329 | Cl | H | Cl | -CH ₃ |  |
| 330 | Cl | H | Cl | -CH ₃ |  |
| 331 | Cl | H | Cl | -CH ₃ |  |
| 332 | Cl | H | Cl | -CH ₃ |  |
| 333 | Cl | H | Cl | -CH ₃ |  |
| 334 | Cl | H | Cl | -CH ₃ |  .TFA |
| 335 | Cl | H | Cl | -CH ₃ |  |
| 336 | Cl | H | Cl | -CH ₃ |  |
| 337 | Cl | H | Cl | -CH ₃ |  |

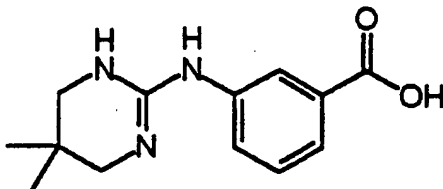
- 583 -

| Example | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ |
|---------|----------------|----------------|----------------|------------------|--|
| 338 | Cl | H | Cl | -CH ₃ |  |
| 339 | Cl | H | Cl | -CH ₃ |  |

- 584 -

Example 361

Preparation of (±) ethyl 3,5-dichloro-β-[[2-[[[3-
[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)-
5 amino]phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoate, trifluoroacetate salt

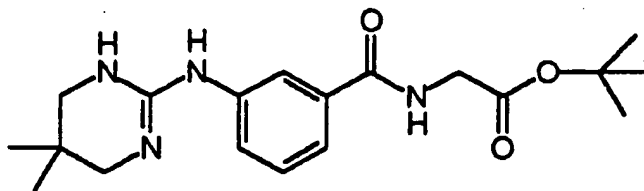
Step A

To a suspension of the 1-(3-carboxyphenyl)-2-thiourea
15 (produced in Example 236, Step A) (10.00 g, 0.051 mol) in
ethanol (100 mL) was added iodomethane (3.5 mL) and heated
at 70°C under nitrogen atmosphere for 2.5 hours. The
reaction mixture was concentrated under reduced pressure,
the residue was triturated with ether containing 10% EtOAc
20 (2 x 100 mL) and the supernatant decanted. The resulting
solid was dried *in vacuo* for 2 hours, dissolved in DMF (75
mL) and added dropwise to a solution of 2,2 dimethyl-1,3
propanediamine (42 g, 0.41 mol) in DMF (20 mL) over a
period of 1 hour. The resulting mixture was heated at
25 80°C under nitrogen atmosphere for 16 hours with
simultaneous trapping of the methylmercaptan in 5% sodium
hypochlorite solution. DMF was distilled *in vacuo*, the
residue was dissolved in water (50 mL) and washed with
diethyl ether (3 x 25 mL). The aqueous phase was
30 acidified with 2N HCl to pH 4.0 when a white precipitate
was obtained. It was filtered, washed with water and
ether and dried to give the desired product 8.0 g (63%)
as a white powder. ¹H-NMR and MS were consistent with the
structure.

- 585 -

Step B

5

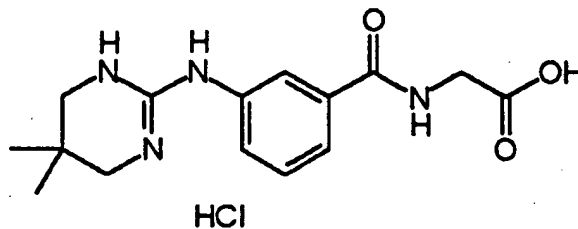


To a suspension of the HCl salt of Step A (1.0 g, 0.0035 mol) in DMF (15 ml), was added N-methylmorpholine (0.46 mL) and cooled to -10°C in an ice-salt bath. This reaction mixture was then treated with isobutyl chloroformate (0.45 mL), stirred at -10°C for 30 minutes, and a solution of the amine generated by the addition of N-methylmorpholine (0.46 mL) to a solution of t-butylglycinate hydrochloride (0.6 g) in DMF (5 mL) at 0°C. The resulting reaction mixture was stirred at -10°C for 1 hour and at room temperature for 16 hours under argon atmosphere. DMF was distilled *in vacuo*, the residue was treated with 5% sodium bicarbonate (25 mL) and EtOAc (25 mL) and stirred at room temperature for 30 minutes. A white precipitate was obtained. The precipitate was filtered, washed with water (2 x 20 mL), and EtOAc (2 x 20 mL), and dried to give the desired compound, 0.58 g (46%). ¹H-NMR and MS were consistent with the structure.

25

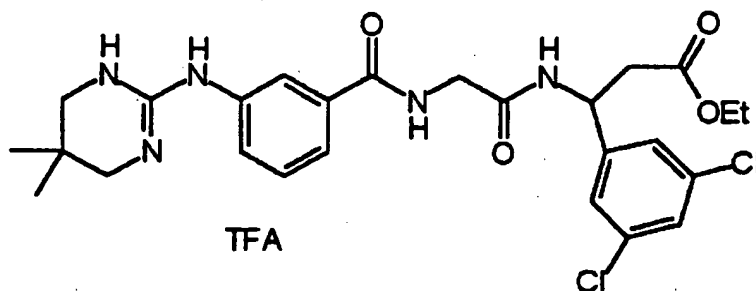
Step C

30



- 586 -

Th product of Step B (0.6 g, 0.0017 mol) was suspended in dioxane (2.0 mL) and treated with 4N HCl in dioxane (0.9 mL) and stirred overnight at room temperature. The reaction mixture was diluted with
5 diethyl ether, filtered, and the residue washed with diethyl ether (3 x 20 mL). The resulting pale yellow solid was dried in a desiccator over NaOH pallets and used as such in the following step, without purification.

10 Step D

To a suspension of HCl salt as prepared in Step C in DMF (10 mL), was added N-methylmorpholine (0.21 mL) and cooled
20 to -10°C in an ice-salt bath. This reaction mixture was then treated with isobutylchloroformate (0.24 mL), stirred at -10°C for 30 minutes, and a solution of the amine generated by the addition of N-methylmorpholine (0.46 mL) to a solution of ethyl DL-3-amino-3-(3,5-dichlorophenyl)-
25 propionate (produced as in Example 1, Steps A and B substituting 3,5-dichlorobenzaldehyde for 3-pyridine carboxaldehyde) (0.6 g, 0.002 mol) in DMF (5 mL) at 0°C. The resulting reaction mixture was stirred at -10°C for 1 hour and at room temperature for 16 hours under argon
30 atmosphere. DMF was distilled in vacuo, the residue was triturated with ether (2 x 25 mL) and the supernatant decanted. The insoluble residue was purified by reverse phase HPLC using a 30 minute gradient of 5-70% CH₃CN in water at a flow rate of 70 mL/minute. The appropriate

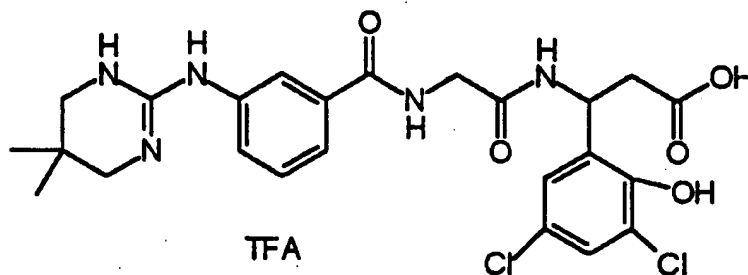
- 587 -

fractions were combined and freeze dried to afford the desired TFA salt, as a pale yellow powder. ¹H-NMR and MS were consistent with the structure.

- 588 -

Example 362

Preparation of (\pm) 3,5-dichloro-2-hydroxy- β -[[2-[[[3-
[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)-
5 amino]phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoic acid, trifluoroacetate salt

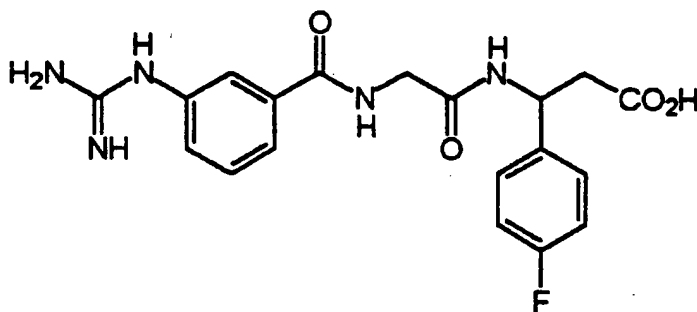


The above compound was prepared by coupling the product of Step C in Example 361 with the product of Example 440, Step A, as described in Example 361. The
20 desired product was isolated by reverse-phase HPLC using a 30 minute gradient of 5-70% CH₃CN in water at a flow rate of 70 mL/minute. The appropriate fractions were combined and freeze dried to afford the desired TFA salt. ¹H-NMR and MS were consistent with the structure.

- 589 -

Example 363

Preparation of β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-fluorobenzenepropanoic acid, trifluoroacetate salt

Step A

A mixture of 4-fluorophenyl bromide (10.0 g, 0.057 mol), tert-butylacrylate (9.52 g, 0.074 mol), palladium acetate (0.13 g, 0.00057 mol), tri-para-tolylphosphine (0.87 g, 0.0029 mol) and triethylamine (5.78 g, 0.057 mol) in 30 mL of DMF was heated at 120°C for 16 hours. The mixture was cooled and treated with 500 mL of water. The aqueous phase was extracted with ethyl acetate (3 x 200 mL) and the organic layer was washed with brine, dried over magnesium sulfate and filtered. The filtrate was concentrated and the residue was purified by chromatography on silica gel (ethyl acetate/hexane, 1:9) to give 10.13 g of product as a yellow oil (80%). The NMR was consistent with the proposed structure.

Analysis Calc'd. for $C_{13}H_{15}FO_2$: C, 70.25; H, 6.80.
Found: C, 69.77; H, 7.08.

- 590 -

Step B

The product from Step A (8.7 g, 0.039 m l) was treated with tert-butanol saturated with ammonia and 3 mL of acetic acid at 110°C and 900 psi in a Parr shaker for 48 hours. The mixture was filtered and concentrated. The residue was dissolved with 200 mL of cold 1N HCl and extracted with ethyl acetate. The aqueous phase was then basified with potassium carbonate and extracted with methylene chloride (2 x 200 mL). The combined extracts were washed with brine, dried over magnesium sulfate and filtered. The filtrate was concentrated to give 4.23 g of a yellow oil (41%). The structural assignment was supported by the NMR spectrum.

15 Step C

To a solution of the compound of Example M (1.0 g, 0.0037 mol) in 10 mL of DMF was added N-methylpiperidine (0.42 g, 0.0037 mol) rapidly. The mixture was stirred at room temperature for 20 minutes, then treated with isobutyl chloroformate at 0°C. After 15 minutes, a solution of the product from Step B in 3 mL of DMF was added. The reaction mixture was allowed to warm to room temperature and stirred overnight. Dimethylformamide was removed in vacuo and the residue was purified by reverse phase HPLC [acetonitrile/water (containing 0.5% of TFA)] to give 0.97 g of a pale yellow solid (44%):

Analysis Calc'd. for $C_{23}H_{27}N_5O_4F \cdot 1.0 H_2O \cdot 1.0 TFA$:

C, 50.93; H, 5.30; N, 11.88.

Found: C, 50.61; H, 4.92; N, 11.74.

30

Step D

To a suspension of the product from Step C in 10 mL of methylene chloride at 0°C was added 6 mL of TFA. The mixture was stirred at room temperature for 4 hours.

- 591 -

Solvent was removed and the residue was purified by reverse phase HPLC [acetonitrile/water (containing 0.5% of TFA)] to give 0.75 g of the title compound as a white solid (75%):

5 Analysis Calc'd. for $C_{19}H_{20}N_3O_4F \cdot 1.5$ TFA:

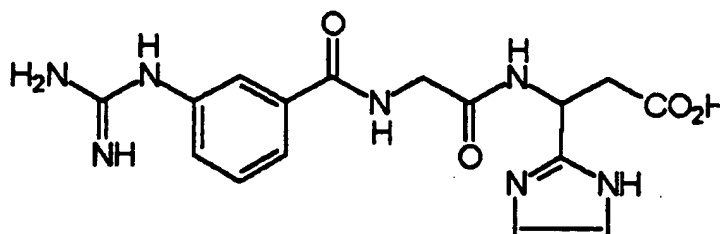
C, 46.16; H, 3.79; N, 12.23.

Found: C, 45.86; H, 3.68; N, 12.23.

- 592 -

Example 364

Preparation of (\pm) β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
1H-imidazole-2-propanoic acid,
tris(trifluoroacetate) salt

Step A

A solution of 2-imidazolecarboxaldehyde (6.0 g, 0.063 mol) and (tert-butylcarbonylmethylene)triphenylphosphorane (29.4 g, 0.078 mol) in 150 mL of tetrahydrofuran was heated at 55°C overnight. The clear solution was cooled and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (ethyl acetate/hexane, 8:2) to give 9.7 g of product (1:1 E/Z mixture) as a white solid (79%): Analysis Calc'd. for $C_{10}H_{14}N_2O_2$:

C, 61.84; H, 7.27; N, 14.42.

Found: C, 61.52; H, 7.39; N, 14.21.

Step B

To a suspension of prewashed sodium hydride (0.62 g, 0.026 mol) in 40 mL of dry dimethylformamide was added the product from Step A slowly. After 30 minutes, 2-(trimethylsilyl)ethoxymethyl chloride was added and the reaction mixture was stirred at room temperature for 2 hours. Water was added and the aqueous phase was extracted with ethyl acetate. The organic layer was washed with brine, dried over magnesium sulfate and filtered. The filtrate was concentrated and the residue

- 593 -

purified by chromatography on silica gel (ethyl acetate/hexane, 1:1) to give 3.54 g of E isomer as a colorless oil and 2.66 g of Z isomer as a white solid (73%). Analysis Calc'd. for $C_{16}H_{28}N_2O_3Si$:

5 C, 59.22; H, 8.70; N, 8.63.

Found: C, 58.94; H, 9.12; N, 8.53.

Step C

To a solution of N-benzyl(trimethylsilyl)amine
10 (2.16 g, 0.012 mol) in 30 mL of dry tetrahydrofuran at
-78°C was added n-butyllithium (0.012 mol) slowly. After
30 minutes, a solution of the product of Step B (2.6 g,
0.008 mol) in 15 mL of tetrahydrofuran was added and the
15 reaction mixture was stirred at this temperature for 2.5
hours. The reaction was then quenched with a solution of
acetic acid in tetrahydrofuran, followed by addition of
saturated sodium bicarbonate to pH 9. The aqueous phase
was extracted with ethyl acetate and the organic layer was
20 washed with brine, dried over magnesium sulfate and
filtered. The filtrate was concentrated and purified by
chromatography on silica gel (ethyl acetate/hexane, 6:4)
to give 1.96 g of product as a clear oil (60%).

Analysis Calc'd. for $C_{23}H_{37}N_3O_3Si$:

C, 64.00; H, 8.64; N, 9.73.

25 Found: C, 63.72; H, 8.85; N, 9.73.

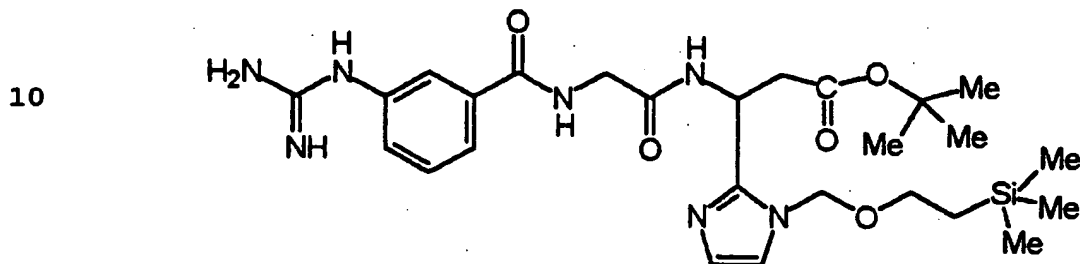
Step D

To a solution of the product from Step C (5.4 g,
0.0125 mol) and ammonium formamide (7.89 g, 0.125 mol) in
30 150 mL of methanol was added Pd/C (170 mg). The mixture
was stirred at reflux for 3 hours. The catalyst was
filtered through celite and the filtrate was concentrated.
The residue was dissolved in 400 mL of water, saturated
with potassium carbonate, extracted with ethyl acetate.

- 594 -

The organic layer was washed with brine, dried over magnesium sulfate and filtered. The filtrate was concentrated to give 3.9 g of product as a colorless oil (91%). The NMR spectrum indicated that the compound was of sufficient purity for the next step.

Step E



The above compound was synthesized under the same conditions as described in Step C of Example 363. The crude product was purified by reverse phase HPLC [acetonitrile/water (containing 0.5% of TFA)] to give 1.5 g of product as a yellow solid (60%):

20 Analysis Calc'd. for $C_{26}H_{41}N_7O_5Si \cdot 2.5$ TFA:

C, 44.07; H, 5.19; N, 11.61.

Found: C, 44.24; H, 5.14; N, 11.91.

Step F

25 The title compound was obtained from the product of Step E following the procedure described in Step D of Example 363. The crude product was purified by reverse phase HPLC [acetonitrile/water (containing 0.5% of TFA)] to give 0.35 g of the title compound as a yellow solid (24%):

30

Analysis Calc'd. for $C_{16}H_{19}N_7O_4 \cdot 3.0$ TFA:

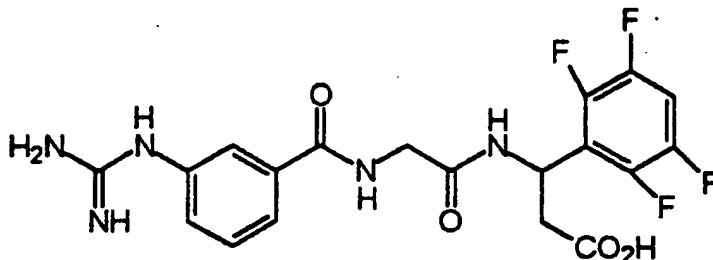
C, 36.93; H, 3.10; N, 13.70.

Found: C, 37.76; H, 2.95; N, 14.22.

- 595 -

Example 365

Preparation of (\pm) β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
5 2,3,5,6-tetrafluorobenzenepropanoic acid,
trifluoroacetate salt



The above compound was made by following the reaction
15 sequence described in Example 364 Step A and Step C to
Step F. The structure was confirmed by the NMR spectrum.
Analysis Calc'd. for $C_{19}H_{17}N_5O_4F_4 \cdot 1.5$ TFA:

C, 42.18; H, 2.98; N, 11.18.

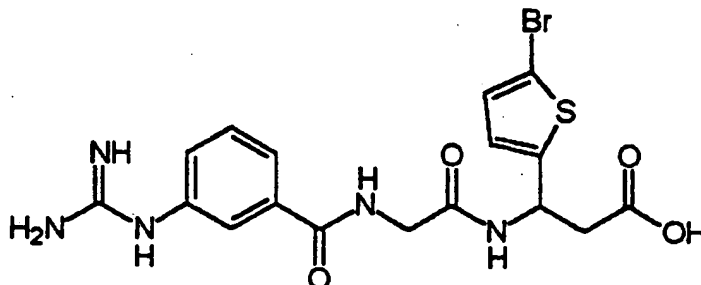
Found: C, 42.24; H, 3.07; N, 11.12.

20

- 596 -

Example 366

Preparation of β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
5 -5-bromothiophene-2-propanoic acid,
trifluoroacetate salt, monohydrate



15

A solution of the product of t-butyl ester of the
above compound (prepared according to analogous
methodology as described herein) (1.0 g, 1.91 mmol) and
20 trifluoroacetic acid (14.8 g, 10.0 ml, 13.0 mmol) in
dichloromethane (25 ml) was stirred at 0°C for 30 minutes.
The reaction mixture was allowed to warm to room
temperature and stirred for 6 hours. The solvent was
removed under reduced pressure. The crude product was
25 purified by HPLC (acetonitrile, water, trifluoroacetic
acid) to give pure title compound (0.43 g, 38%) as a white
solid.

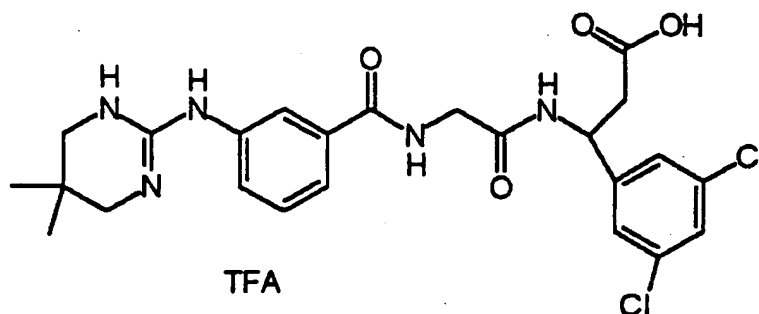
Analysis Calc'd. for $C_{17}H_{18}N_5O_4SBr \cdot CF_3COOH \cdot H_2O$:

30 Found: C, 38.01; H, 3.53; N, 11.67; S, 5.34
C, 38.07; H, 3.23; N, 11.48; S, 4.99

- 597 -

Example 367

Preparation of (\pm) 3,5-dichloro- β -[[2-[[[3-
[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-
2-yl)amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoic acid,
trifluoroacetate salt

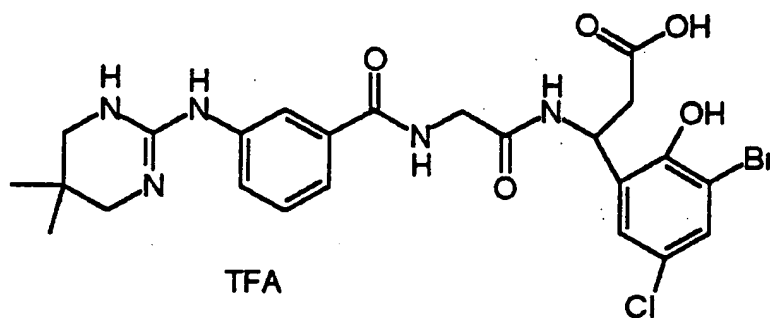


The ethyl ester prepared in Example 361, Step D (0.22 g) was hydrolyzed to the acid using 1M LiOH, (1.8 mL) in acetonitrile (0.2 mL), followed by acidification and purification by reverse-phase HPLC to give 0.18 g of the acid as pale yellow powder. ^1H NMR and MS were consistent with the structure.

- 598 -

Example 368

Preparation of (±) 3-bromo-5-dichloro-2-hydroxy-
β-[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-
5 dimethylpyrimidin-2-yl)amino]phenyl]-
carbonyl]amino]acetyl]amino]benzene-
propanoic acid, trifluoroacetate salt



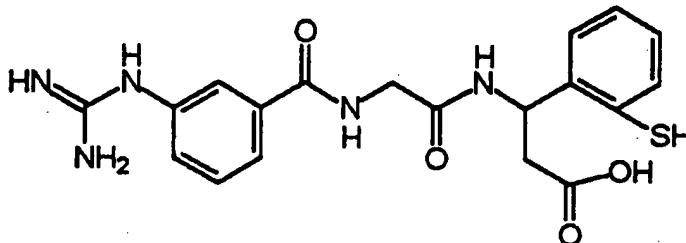
The above compound was prepared by coupling the acid
prepared in Example 361, Step C, (0.6 g) with the product
20 of Example 233, Step B (0.5 g) according to the procedure
described in Example 361. The desired product was
isolated by reverse-phase HPLC to give 0.38 g of the above
compound as a pale yellow powder. ¹H NMR and MS were
consistent with the structure.

25

- 599 -

Example 370

Synthesis of β -[[2-[[[3-[(aminoimin methyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-2-mercaptobenzenepropanoic acid, lithium salt

Step A

Synthesis of S-Phenyl Thiocinnamate: A solution of cinnamoyl chloride (14.6 g, 87.68 mmol) in dichloromethane (100 mL) was added to a solution of thiophenol (9.55 g, 86.68 mmol) and pyridine (7 mL) in dichloromethane (150 mL) in an ice-water bath. After 18 hours at room temperature, the reaction mixture was washed with dilute hydrochloric acid (100 mL, 1N), brine (100 mL), dried (MgSO₄) and was concentrated to afford 19.0 g (91%) of the desired thioester as a crystalline solid.

Step B

Synthesis of Thiocoumarin: A mixture of S-phenyl thiocinnamate (14.0 g, 58.25 mmol) and aluminum chloride (39 g) was stirred and heated at 85°C for 3 hours. The hot reaction mixture was poured carefully over ice, then was extracted with ethyl acetate (3 x 300 mL), washed with brine (200 mL), dried (MgSO₄) and was concentrated. The residue was recrystallized from hexane-ethyl acetate to afford 5.2 g (52%) of the desired product as pale yellow crystals.

- 600 -

Step C

Synthesis of 4-Amino-3,4-Dihydr thiocoumarin
Hydrochloride Salt: Lithium hexamethyldisilazane (10.22 mL, 1N, 10.22 mmol) was added slowly to a solution of
5 thiocoumarin (1.41 g, 8.52 mmol) in tetrahydrofuran (20 mL) at -78°C. After 45 minutes, the reaction mixture was warmed up to 0°C, then was quenched with glacial acetic acid (0.511 g). After 10 minutes, the reaction mixture
10 was partitioned between ethyl acetate (100 mL) and sodium bicarbonate (100 mL). The organic layer was dried (MgSO₄) and was concentrated. The residue obtained was dissolved in ether (100 mL) and dioxane/HCl (20 mL, 4N) was added. The precipitate formed was filtered and the solid was
15 dried in vacuo to afford (0.50 g, 27%) of the desired product as a yellow powder.

Step D

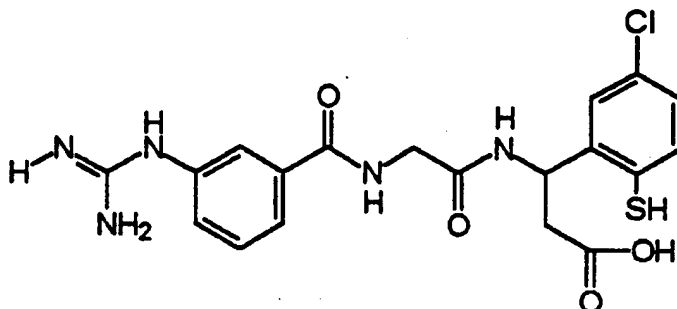
A solution of m-guanidinohippuric acid (0.506 g, 1.855 mmol) in dimethylformamide (5 mL) and N-
20 methylmorpholine (0.187 g, 1.855 mmol) was cooled to 0°C and was stirred for 15 minutes. Isobutylchloroformate (0.253 g, 1.855 mmol) was added in three portions. After 10 minutes, 4-amino-3,4-dihydrothiocoumarin hydrochloride (0.404 g, 1.855 mmol) was added in one portion followed by
25 N-methylmorpholine (0.187 g, 1.855 mmol). The reaction mixture was stirred for 18 hours at room temperature. The reaction mixture was concentrated and the residue was dissolved in tetrahydrofuran/water (1:1, 5 mL) and was
30 chromatographed (reverse phase, 95:5 water: acetonitrile over 60 minutes to 30:70 water: acetonitrile containing 0.1% TFA). The eluents were lyophilized to afford 0.300 g of the title compound as a pale yellow powder.

Proton NMR and MS were consistent with the desired product.

- 601 -

Example 371

Preparation of (\pm) β -[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-5-
chloro-2-mercaptobenzenepropanoic acid,
dilithium salt

Step A

Synthesis of S-(4-Chlorophenyl) Thiocinnamate: A solution of cinnamoyl chloride (26.0 g, 156.3 mmol) in dichloromethane (100 mL) was added to a solution of thiophenol (22.6 g, 156.3 mmol) and pyridine (12.6 mL) in dichloromethane (200 mL) in an ice-water bath. After 18 hours at room temperature, the reaction mixture was washed with dilute hydrochloric acid (100 mL, 1N), brine (100 mL), dried (MgSO_4) and was concentrated to afford 41.0 g (96%) of the desired thioester as a crystalline solid.

Step B

Synthesis of 6-Chlorothiocoumarin: A powdered mixture of S-(4-chlorophenyl) thiocinnamate (19.4 g) and aluminum chloride (52 g) was stirred and heated at 125°C for 3 hours. The hot reaction mixture was poured carefully over ice/water, then was extracted with ethyl acetate (3x300 mL), washed with brine (200 mL), dried (MgSO_4) and was concentrated. The residue was triturated

- 602 -

with hexane/ethyl acetate to afford 2.0 g (14%) of the desired product as pale yellow crystals.

Step C

5 Synthesis of 4-amino-6-chloro-3,4-dihydrothiocoumarin hydrochloride salt: Lithium hexamethyldisilazane (6.4 mL, 1N, 6.4 mmol) was added slowly to a solution of 6-chlorothiocoumarin (1.05 g, 5.345 mmol) in tetrahydrofuran (20 mL) at -78°C. After 45 minutes, the
10 reaction mixture was warmed up to 0°C, then was quenched with glacial acetic acid (0.321 g). After 10 minutes, the reaction mixture was partitioned between ethyl acetate (100 mL) and sodium bicarbonate (100 mL). The organic layer was dried (MgSO₄) and was concentrated. The residue
15 obtained was dissolved in ether (100 mL) and dioxane/HCl (20 mL, 4N) was added. The precipitate formed was filtered and the solid was dried in vacuo to afford (0.80 g, 60%) of the desired product as a yellow powder.

20 Step D

 A solution of m-guanidinohippuric acid (0.548 g, 2.0 mmol) in dimethylformamide (5 mL) and N-methylmorpholine (0.220 mL, 2.0 mmol) was cooled to 0°C and was stirred for 15 min. Isobutylchloroformate (0.260 mL, 2.0 mmol) was
25 added in three portions. After 10 minutes, 4-amino-6-chloro-3,4-dihydrothiocoumarin hydrochloride (0.50 g, 2.0 mmol) was added in one portion followed by N-methylmorpholine (0.220 mL, 2.0 mmol). The reaction mixture was stirred for 18 hours at room temperature. The
30 reaction mixture was concentrated and the residue was dissolved in tetrahydrofuran/water (1:1, 5 mL) and was chromatographed (reverse phase, 95:5 water: acetonitrile over 60 minutes to 30:70 water: acetonitrile containing 0.1% TFA). The eluents were basified with an aqueous

- 603 -

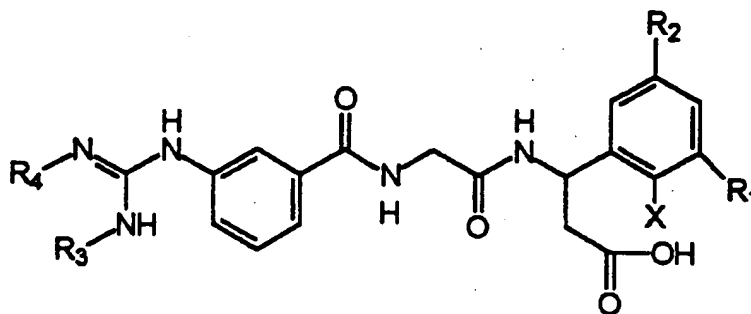
solution of lithium hydroxide and then was lyophilized to afford 0.300 g of the title compound as a pale yellow powder.

MS and NMR were consistent with the proposed
5 structure.

- 604 -

Example 372

The following compounds are prepared according to the methodology described in Examples 370-371.



X=SH; $R_1, R_2 = Cl$; $R_3, R_4 = H$

X=SH; $R_1, R_2 = F$; $R_3, R_4 = H$

X=SH; $R_1, R_2 = Me$; $R_3, R_4 = H$

X=SH; $R_1, R_2 = CF_3$; $R_3, R_4 = H$

X=SH; $R_1, R_2 = Br$; $R_3, R_4 = H$

X=SH; $R_1 = H$, $R_2 = F$; $R_3, R_4 = H$

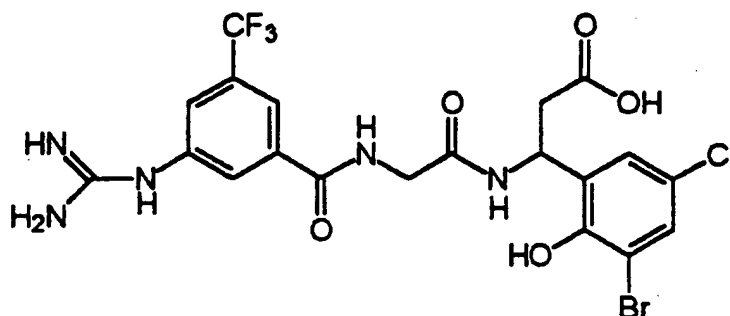
X=SH; $R_1 = H$, $R_2 = Br$; $R_3, R_4 = H$

X=SH; $R_1 = H$, $R_2 = CF_3$; $R_3, R_4 = H$

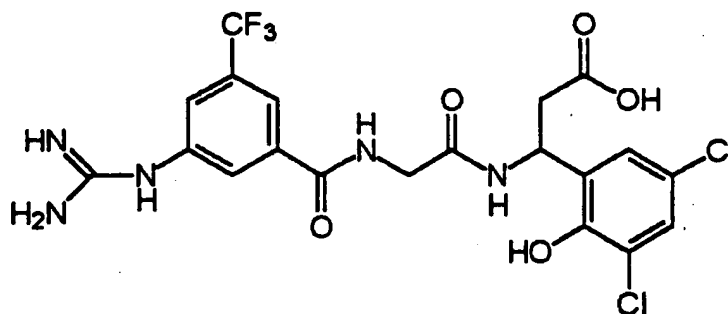
X=SH; $R_1 = H$, $R_2 = CH_3$; $R_3, R_4 = H$

and the above compounds wherein R_3 and R_4 together are $(CH_2)_3$ or $(CH_2)_2$.

- 605 -

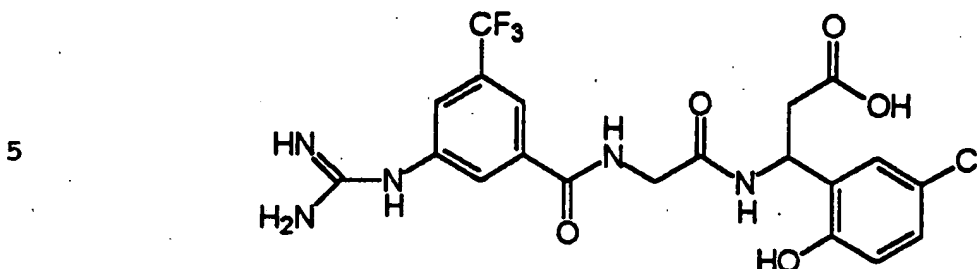
EXAMPLE 374

10 The above compound is prepared by reacting the
compound prepared in Example 233, Step B with 3-guanidino-
5-trifluoromethylhippuric acid (prepared according to the
15 procedure of Example 38) using substantially the
proportions and procedure of Example N, Step 3 and
substituting 3-guanidino-5-trifluoromethylhippuric acid
hydrochloride for GIHA HCl. The desired product is
isolated by C-18 RPHPLC.

EXAMPLE 375

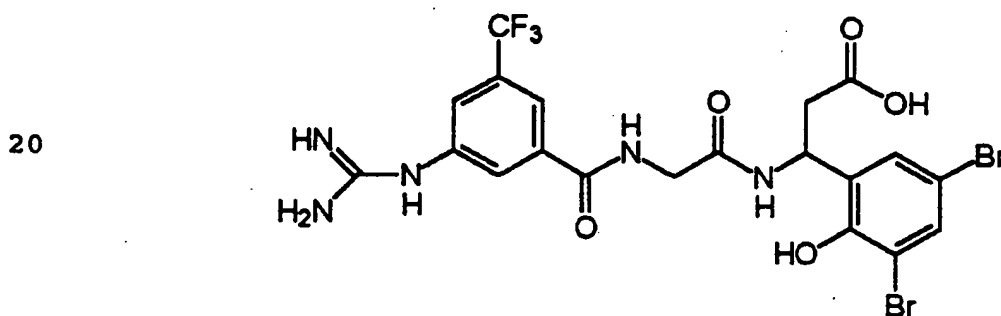
20
25
30 The above compound is prepared using the procedure of
Example 374 and substituting (RS)-4-amino-6,8-dichloro-
hydrocoumarin hydrochloride prepared in Example 237 for
the compound of Example 233, Step B. The desired product
is isolated by C-18 RPHPLC.

- 606 -

EXAMPLE 376

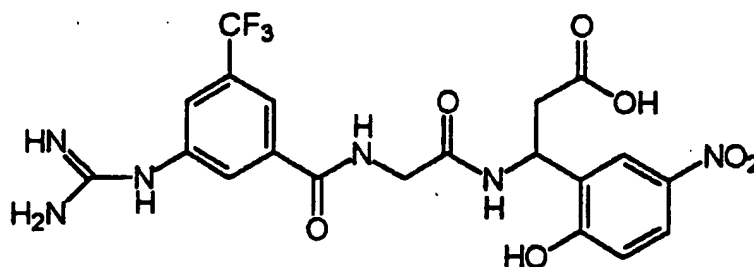
10 The above compound is prepared using the procedure of Example 374 and substituting (RS)-4-amino-6-chloro-hydrocoumarin hydrochloride prepared in Example 231 for the compound of Example 233, Step B. The desired product is isolated by C-18 RPHPLC.

15

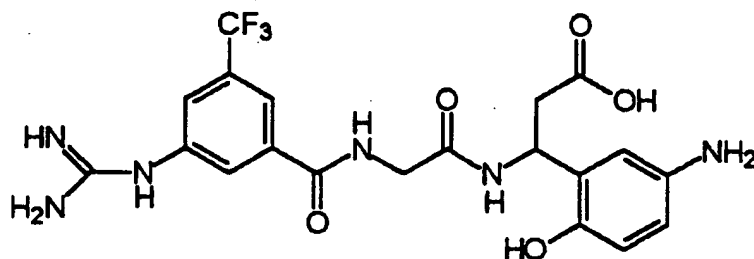
EXAMPLE 377

25 The above compound is prepared using the procedure of Example 374 and substituting the compound prepared in Example 227 for the compound of Example 233, Step B. The desired product is isolated by C-18 RPHPLC.

- 607 -

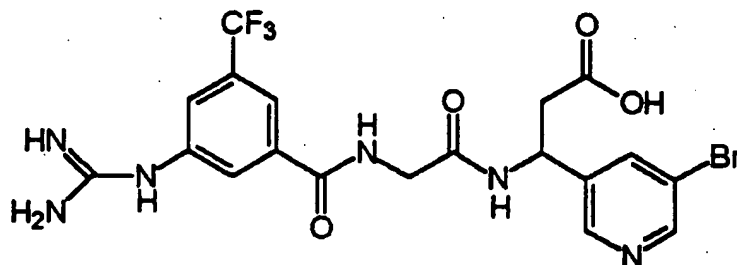
EXAMPLE 378

5
10 The above compound is prepared using the procedure of Example 374 and substituting (RS)-4-amino-6-nitro-hydrocoumarin hydrochloride prepared in Example 226 for the compound prepared in Example 233, Step B. The desired product is isolated by C-18 RPHPLC.

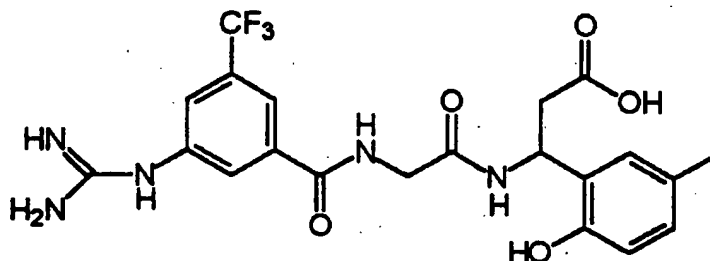
EXAMPLE 379

20
25 The above compound is prepared from the product of Example 378 using the conditions of Example 234. The desired product is isolated by C-18 RPHPLC.

- 608 -

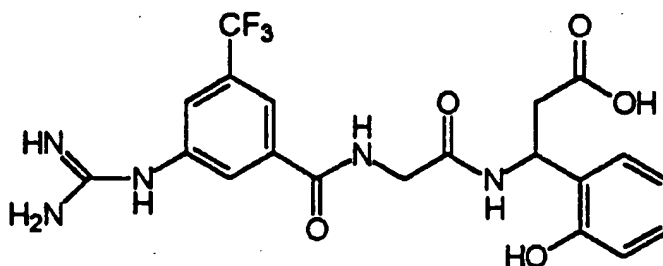
EXAMPLE 380

The above compound is prepared using the procedure of Example 374 and substituting the compound prepared in Example 235, Steps A-C and two equivalents of NMM in the coupling step for the compound prepared in Example 233, Step B and one equivalent of NMM. The desired product is isolated by C-18 RPHPLC.

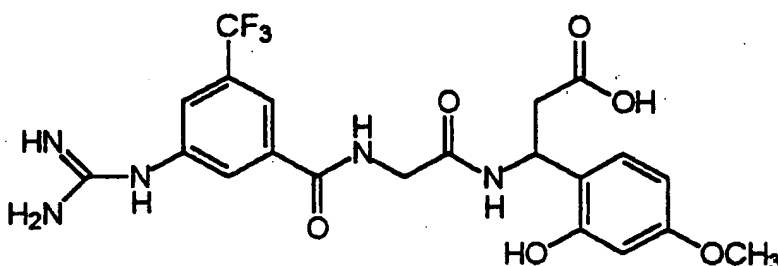
EXAMPLE 381

The above compound is prepared using the procedure of Example 374 and substituting (RS)-4-amino-6-methyl-hydrocoumarin hydrochloride (prepared in Example 88) for the compound prepared in Example 233, Step B. The desired product is isolated by C-18 RPHPLC.

- 609 -

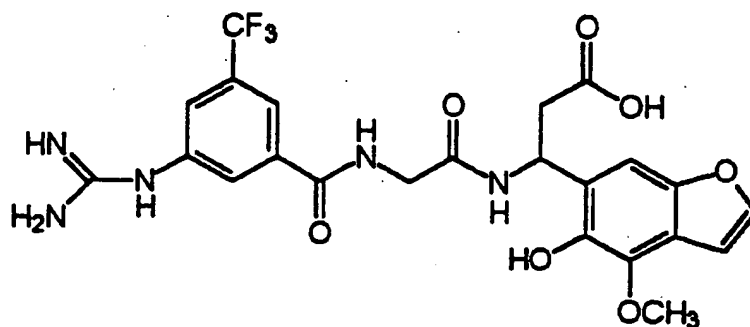
EXAMPLE 382

The above compound is prepared using the procedure of Example 374 and substituting (RS)-4-amino-hydrocoumarin hydrochloride (prepared in Example 87) for the compound prepared in Example 233, Step B. The desired product is isolated by C-18 RPHPLC.

EXAMPLE 383

The above compound is prepared using the procedure of Example 374 and substituting (RS)-4-amino-7-methoxy-hydrocoumarin hydrochloride (prepared in Example 222) for the compound prepared in Example 233, Step B. The desired product is isolated by C-18 RPHPLC.

- 610 -

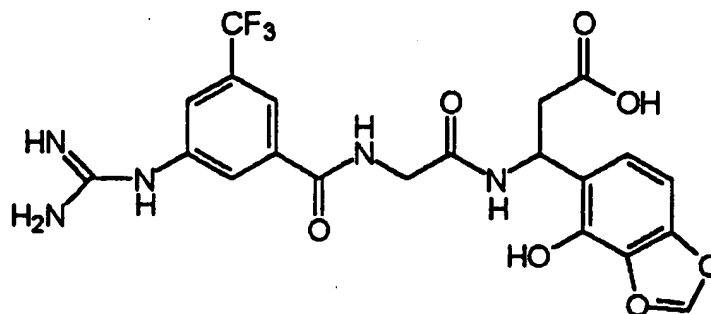
EXAMPLE 384

10

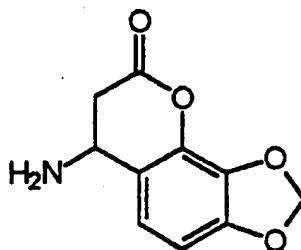
The above compound is prepared using the procedure of Example 374 and substituting (RS)-4-amino-8-methoxy-hydropsoresalen hydrochloride (prepared in Example 223) for the compound prepared in Example 233, Step B. The desired product is isolated by C-18 RPHPLC.

15

- 611 -

EXAMPLE 385Step A

10 Preparation of



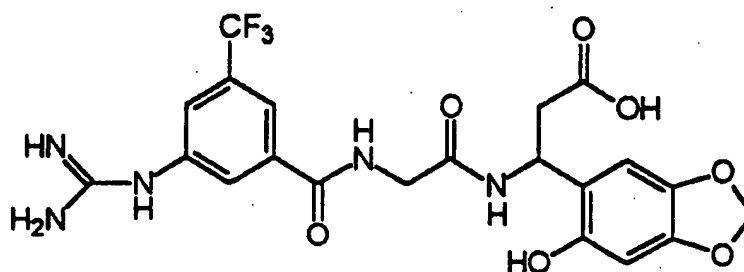
The above compound is prepared from 7,8-methylenedioxy-coumarin (which may be prepared from 7,8-dihydroxy-chromen-2-one according to P. Castillo, J.C. Rodriguez-Ubis, and F. Rodriguez, *Synthesis*, 10, 839-840 (1986)) using the procedure of Example 233, Steps A and B.

Step B

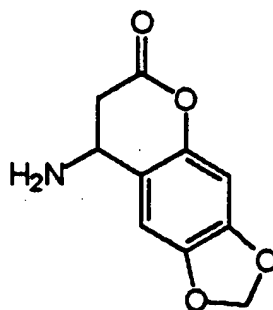
The above Example compound is prepared using the procedure of Example 374, substituting the hydrochloride salt of the product of Step A for the compound prepared in Example 233, Step B. The desired product is isolated by C-18 RPHPLC.

30

- 612 -

EXAMPLE 386Step A

10 Preparation of



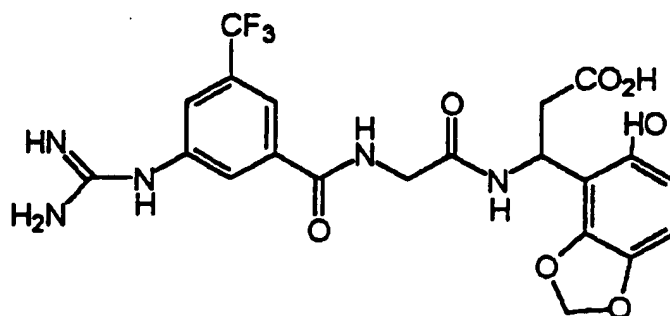
The above compound is prepared from 6,7-methylenedioxy-coumarin [which may be prepared from 6,7-dihydroxy-chromen-2-one according to Spaeth, et al., Chem. Ber., 70, 702 (1937)] using the procedure of Example 233, Steps A and B.

25 Step B

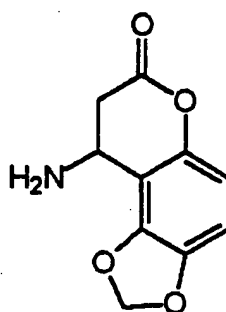
The above Example compound is prepared using the procedure of Example 374 and substituting the hydrochloride salt of the product of Step A for the compound prepared in Example 233, Step B. The desired product is isolated by C-18 RPHPLC.

30

- 613 -

EXAMPLE 387Step A

10 Preparation of

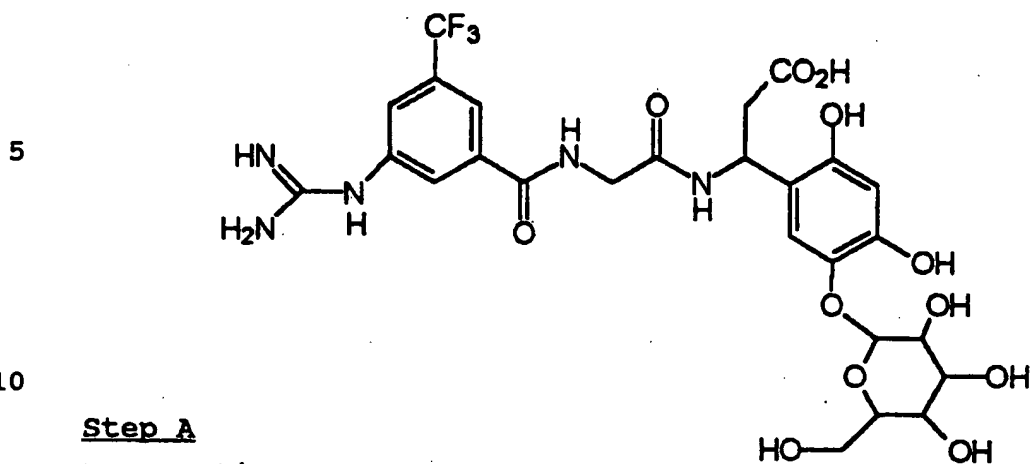


20 The above compound is prepared from 5,6-methylenedioxy-coumarin [prepared from 5,6-dihydroxy-chromen-2-one according to P. Castillo, J.C. Rodriguez-Ubis, and F. Rodriguez, *Synthesis* 10, 839-840 (1986)] using the procedure of Example 233, Steps A and B.

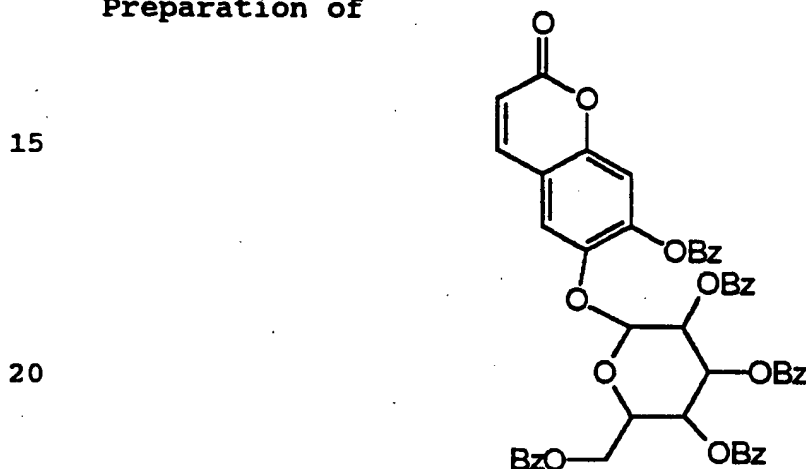
25 Step B

The above Example compound is prepared using the procedure of Example 374, substituting the hydrochloride salt of the hydrochloride salt of the product of Step A for the compound prepared in Example 233, Step B. The
30 desired product is isolated by C-18 RPHPLC.

- 614 -

EXAMPLE 388Step A

Preparation of



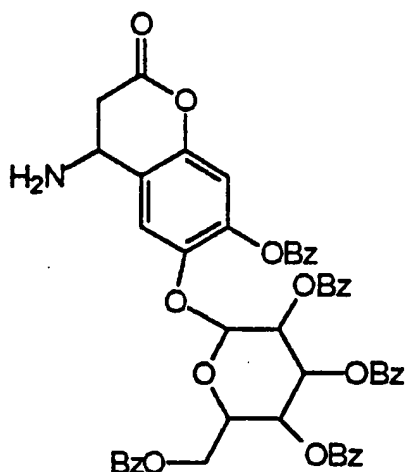
The above compound may be prepared by reacting
25 esculin (Aldrich, rendered substantially free from water
of hydration by storage of P_2O_5 in a vacuum dessicator)
according substantially to the procedure of S. Kato, et
al., *Bull. Chem. Soc. Jap.*, 54, 6, 1981, 1895-1896, for
the conversion of phenyl- α -D-glucoparanoside to phenyl
30 2,3,4,6-tetra-O-benzyl- α -D-glucoparanoside and
substituting the appropriate molar quantities of reagents
to effect complete conversion of esculin to the above
compound. The desired product may be isolated by standard
silica gel chromatography or by preparative C-18 RPHPLC.

- 615 -

Step B

5

10

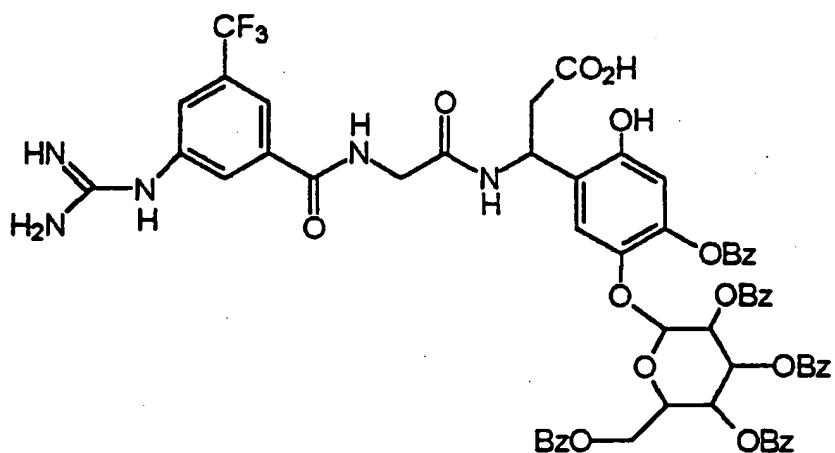


The above compound is prepared using the procedure of Example 233, Step B and substituting the product of Step A for the product of Example 233, Step A.

Step C

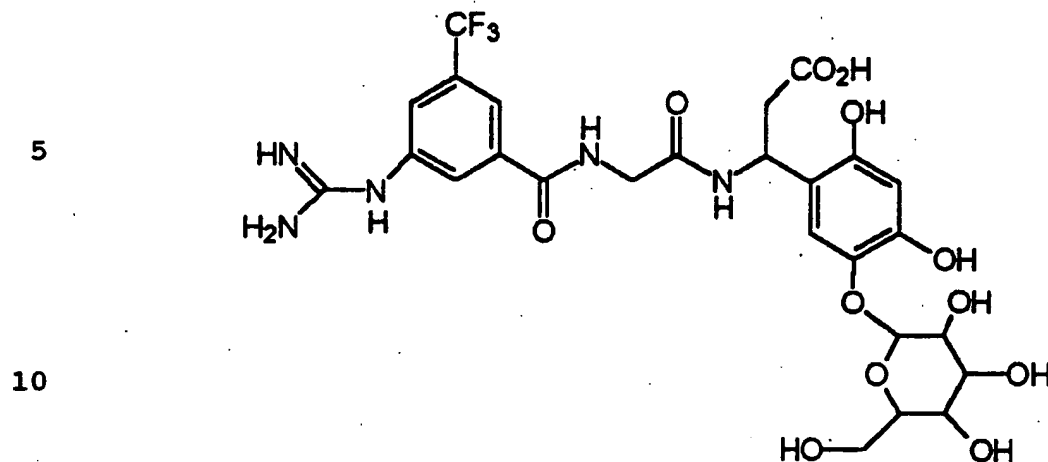
20

25



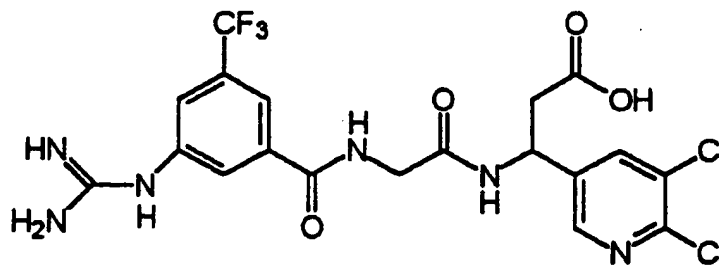
The above compound is prepared using the procedure of Example 374, substituting the hydrochloride salt of the product of Step B for the compound prepared in Example 233, Step B. The desired product is isolated by C-18 RPHPLC.

- 616 -

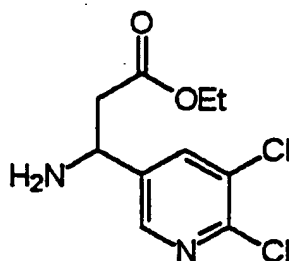
Step D

The above compound is prepared by taking the product of Step C, dissolving in a suitable solvent (e.g. aqueous ethanol), transferring to a Fischer-Porter pressure bottle equipped with an inlet and outlet valve, pressure gauge and pressure relief valve and removing the benzyl groups by standard catalytic hydrogenolysis procedure: 5% Pd on carbon catalyst and hydrogen atmosphere until the debenzylation reaction is substantially complete. The desired product is isolated by C-18 RPHPLC.

- 617 -

EXAMPLE 389Step A

Preparation of

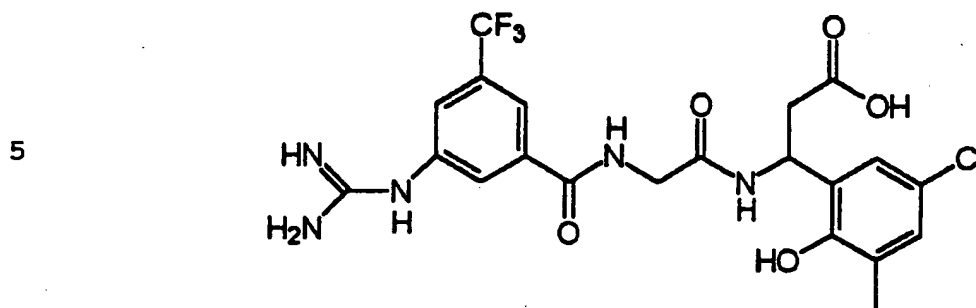


The above compound is prepared using substantially the procedure of Example 235, Steps A-C.

Step B

The above Example compound is prepared using substantially the procedure of Example 235, Steps D and E and is isolated using preparative C-18 RPHPLC.

- 618 -

EXAMPLE 390Step A

10 Preparation of 4-chloro-2-iodophenol



The above compound is prepared according to the
procedure of K.J. Edgar and S.N. Falling, *J. Org. Chem.*,
20 55, 16, 1990, 5287-5291.

Step B

25 Preparation of 5-chloro-3-iodosalicylaldehyde

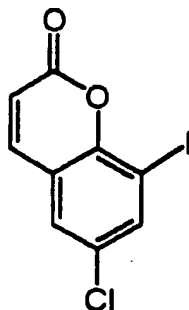


4-chloro-2-iodophenol prepared in Step A is converted
to the salicylaldehyde using the procedure of
G. Casiraghi, et al., *J.C.S. Perkin I*, 1978, 318-321.

- 619 -

Step C

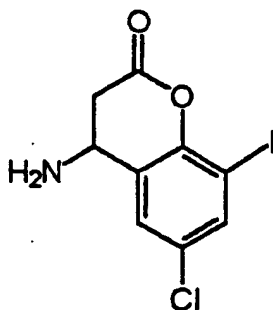
Preparation of 6-chloro-8-iodocoumarin



5-chloro-3-iodosalicylaldehyde is converted into the corresponding coumarin, 6-chloro-8-iodocoumarin, using substantially the procedure of Example 233, Step A and substituting 5-chloro-3-iodo-salicylaldehyde for 3-bromo-5-chlorosalicylaldehyde. The desired product may be isolated by standard silica gel chromatography or distillation.

Step D

Preparation of (R,S)-4-amino-6-chloro-8-iodo-hydrocoumarin



The above compound is prepared using substantially the procedure of Example 233, Step B and substituting the product of Step C for 3-bromo-5-chlorosalicylaldehyde to give the product as substantially pure hydrochloride salt.

- 620 -

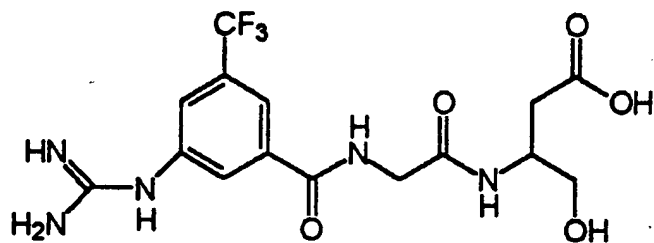
Step E

The above Example compound is prepared using the procedure of Example 274 and substituting the product of Step D for the compound prepared in Example 233, Step B.

- 5 The desired product is isolated by C-18 RPHPLC.

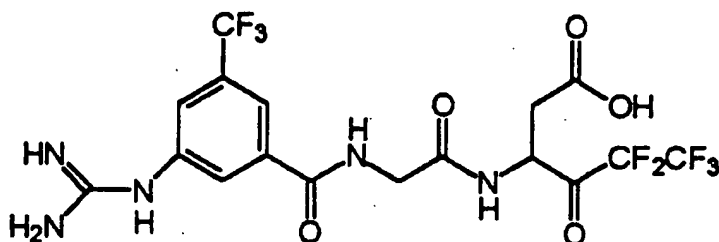
- 621 -

EXAMPLE 391

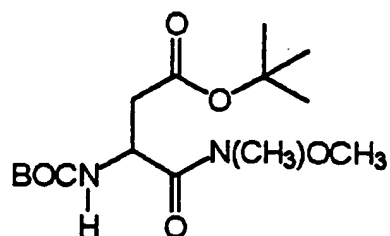


The above compound is prepared using substantially
10 the procedure of Example 86, Step D, substituting 3-
guanidino-5-trifluoromethylhippuric acid hydrochloride for
GIHA HCl. The desired product is isolated by C-18 RPHPLC.

- 622 -

EXAMPLE 392Step A

Preparation of

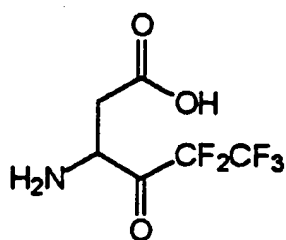


The above compound is prepared using substantially the procedure of Example 235, Step A, substituting BOC-L-aspartic acid-4-tert-butyl ester (Fluka) for 5-bromonicotinic acid.

20

Step B

Preparation of



The above compound is prepared according to substantially the procedure of M.R. Angelastro, et al., *J. Med. Chem.*, 1994, 37, 4538-4554, substituting the product of Step A for Reference compound 2 {(S)-[1-

- 623 -

[methoxymethylamino)carbonyl]-2-methylpropyl carbamic acid,
1,1-dimethyl thyl ester} and deprotecting according to
substantially the procedure employed for obtaining
reference compound 3 to obtain the above compound as the
HCl salt.

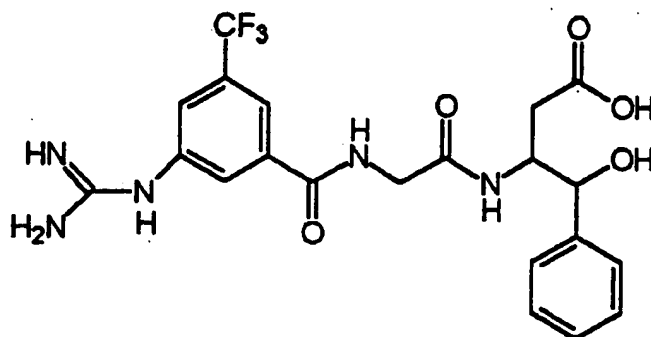
Step C

The above Example compound is prepared using
substantially the procedure of Example 85, Step A,
substituting the product of Step B for glycine t-butyl
ester and substituting 3-guanidino-5-
trifluoromethylhippuric acid hydrochloride for GIHA HCl.
The desired product may be obtained by C-18 RPHPLC.

15

- 624 -

EXAMPLE 393



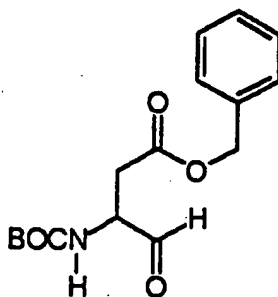
Step A

10 Preparation of 3-N-t-Boc-amino-4-hydroxy-(3S)-butyric acid
benzyl ester

N-t-Boc-L-aspartic acid, β -benzyl ester (10.0 mmole) was dissolved in 10 mL of THF and added dropwise over a period of 30 minutes to a 0°C solution of BH_3 -THF (20 mL, 20.0 mmole), under argon. After the mixture was stirred for an additional 1-2 hours at 0°C, the reaction was quenched by dropwise addition of 10% acetic acid in methanol and the solvent evaporated. The oil residue was dissolved in ethyl acetate and extracted with 1N HCl, water, and 1M NH_4HCO_3 . The ethyl acetate layer was dried (Na_2SO_4) and volatiles evaporated to give an oil was crystallized from isopropanol/hexane (mp 56-57°C): ^1H NMR, CDCl_3 , δ , 1.45 (s, 9H), 2.65 (d, 2H), 3.68 (d, 2H), 5.12 (s, 2H), 5.25 (m, 1H), 7.35 (m, 5H).

Step B

Preparation of



- 625 -

The 3-N-t-Boc-amino-4-hydroxy-butyrlic acid benzyl ester prepared in Step A was oxidized to the corresponding aldehyde using the following Swern oxidation conditions: oxalyl chloride (6.40 g, 20.72 mmole) was dissolved in dry CH₂Cl₂ (25 mL) under argon and cooled to -63°C using a dry ice/chloroform bath. Dry DMSO (g, 41.4 mmole) dissolved in CH₂Cl₂ (12 mL) was added in a dropwise fashion over 15 minutes. The alcohol (6.40 g, 20.7 mmole), dissolved in methylene chloride (50 mL) was then added over 10 minutes. After stirring the reaction mixture for an additional 10 minutes, Et₃N (11.6 mL, 82.9 mmole, 4.0 equivalents) in CH₂Cl₂ (25 mL) was added over 15 minutes. The resulting mixture was stirred for 15 minutes and quenched by addition of water (31 mL). The resulting slurry was poured onto hexanes (250 mL) and the organic layer washed with aqueous KHSO₄. The aqueous layer was extracted with diethyl ether and the combined organic extracts were washed with saturated NaHCO₃, dried (Na₂SO₄) and evaporated to give 5.8 g of a light yellow oil which was substantially the desired aldehyde. A small portion was purified by flash chromatography (hexane: ethyl acetate, Merck 60 silica gel): ¹H NMR (300 MHz), CDCl₃, δ, 1.46 (s, 9H), 2.95 (m, 2H), 4.37 (m, 1H), 5.13 (s, 2H), 5.62 (m, 1H), 7.38 (m, 5H), 9.65 (s, 1H), MS(FAB+) 314.3 (M+Li).

Step C

Preparation of 3-N-t-Boc-amino-4-hydroxy-4-phenyl-(3S)-butyrlic acid benzyl ester

To a diethyl ether (150 mL) solution of aldehyde (5.0 g, 15 mmole) prepared in Step B at -40°C (acetonitrile/dry ice bath) was added in a dropwise fashion a 3.0 M solution of phenyl magnesium bromide in diethyl ether (10.8 mL, 32.6 mmole, 2 equivalents). The resulting mixture was stirred for 15 minutes and warmed to

- 626 -

room temperature. After several minutes the mixture was poured into 1 M K_2HPO_4 . The aqueous layer was extracted again with ether, the combined ether layers washed with aqueous $NaHCO_3$, dried (Na_2SO_4) and evaporated to give an oil (5.66 g) that was used in the next step without further purification: 1H NMR (300 MHz), $CDCl_3$, δ , 1.4 (multiple singlets, 9H), 2.65 (m, 2H), 4.18 (m, 1H), 5.15 (m, 2H), 7.4 (m, 10H); MS(FAB+) 392.4 (M+Li+).

10 Step D

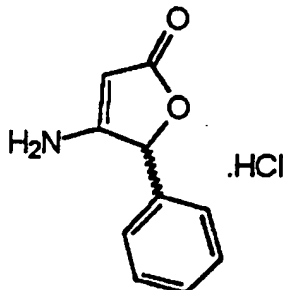
Preparation of 2-phenyl-3-N-t-Boc-amino-5-oxo-3S-furan

The hydroxy-ester product of Step C (5.31 g, 13.8 mmole) was taken up in benzene (100 mL) a catalytic amount of camphor sulfonic acid was added and the solution refluxed (Dean-Stark) for five hours and the solvent removed. Conversion to lactone was 50% so the reaction was reconstituted and refluxed for a further 6 hours. Solvent was removed and the resulting oil taken up in ethyl acetate. The organic layer was washed with aqueous saturated $NaHCO_3$, dried (Na_2SO_4) and evaporated to give a mixture of the desired diastereomeric lactones as a viscous oil in a 2:1 ratio and benzyl alcohol: 1H NMR (300 MHz), $CDCl_3$, δ , 1.35, 1.45 (s, 2:1, 9H), 2.75 (m, 2H), 4.5, 4.75 (m, 2:1, 1H), 4.7 (s, 2H), 5.1 (m, 1H), 5.7 (d, 1H), 7.35 (m, 10H); MS(FAB+) 284.6 (M+Li+).

- 627 -

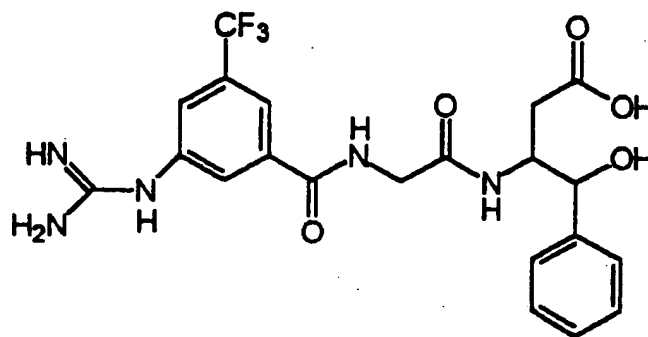
Step E

Preparation of 2-phenyl-3-amino-5-oxo-3S-furane,
hydrochloride



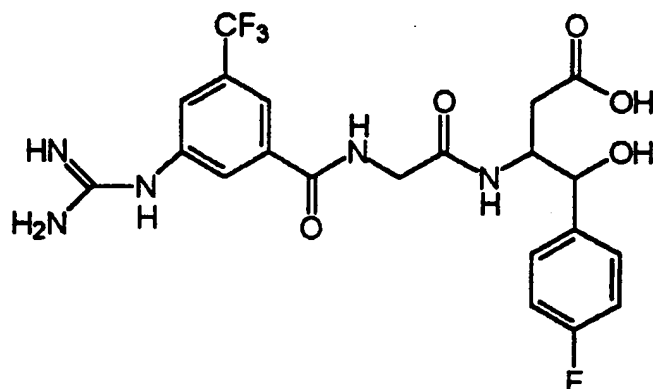
The lactone (0.94 g, 3.4 mmole) prepared in Step D was treated with 4 N HCl in dioxane (20 mL) at room temperature until gas evolution ceased. Excess HCl was removed by evaporation and the desired amino lactone isolated as a white crystalline solid that was dessicated (0.48 g, 66%): ^1H NMR (300 MHz), d_6 DMSO, δ , 3.05 (m, 2H), 4.4 (m, 1H), 5.85 (d, 1H), 7.4 (s, 5H), 8.2 (bs, 3H); MS(FAB+) 178 (M+H+).

- 628 -

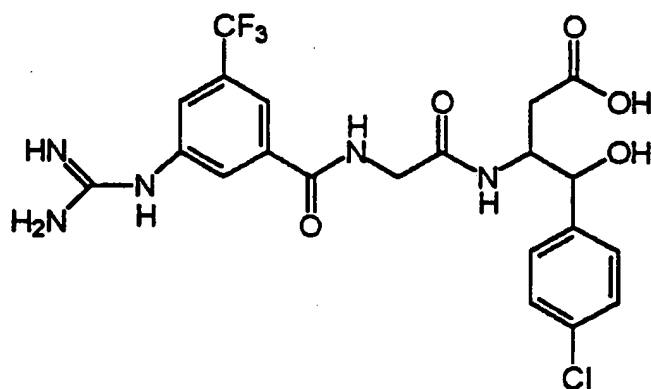
Step F**Preparation of**

The above compound is prepared using substantially the procedure of Example 374, substituting the product of Step E for the compound prepared in Example 233, Step B. The desired product is isolated by C-18 RPHPLC.

- 629 -

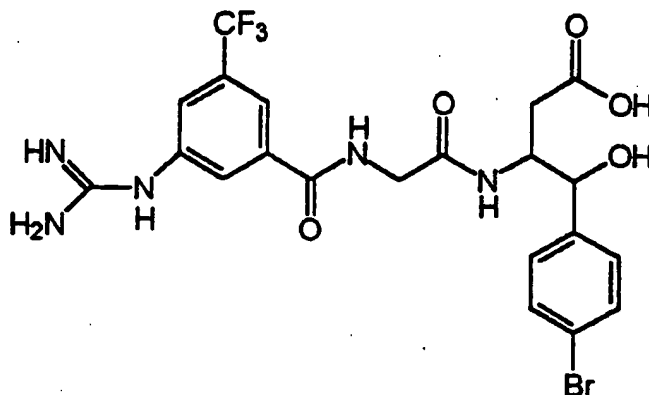
EXAMPLE 394

The above compound is prepared following substantially the procedure of Example 393, substituting 4-fluorophenyl magnesium bromide for phenyl magnesium bromide in Step C.

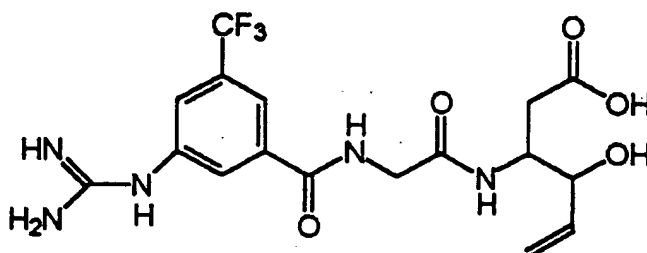
EXAMPLE 395

The above compound is prepared following substantially the procedure of Example 393, substituting 4-chlorophenyl magnesium bromide for phenyl magnesium bromide in Step C.

- 630 -

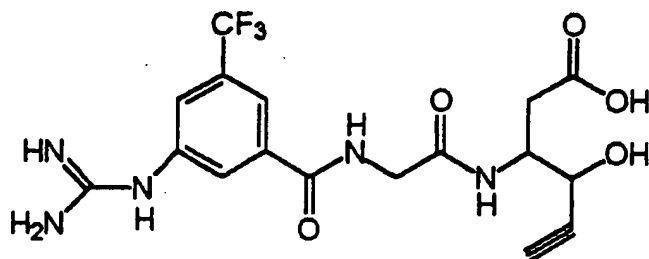
EXAMPLE 396

The above compound is prepared following substantially the procedure of Example 393, substituting 4-bromophenyl magnesium bromide for phenyl magnesium bromide in Step C.

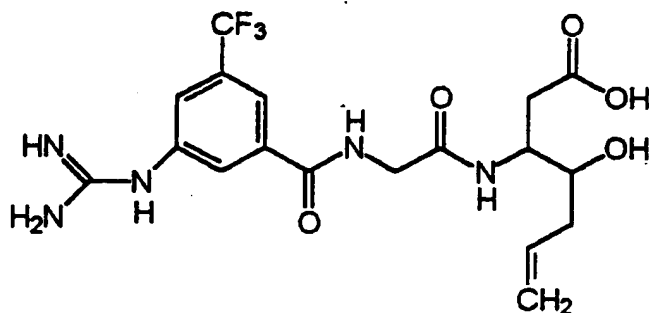
EXAMPLE 397

The above compound is prepared following substantially the procedure of Example 393, substituting vinyl magnesium bromide for phenyl magnesium bromide in Step C.

- 631 -

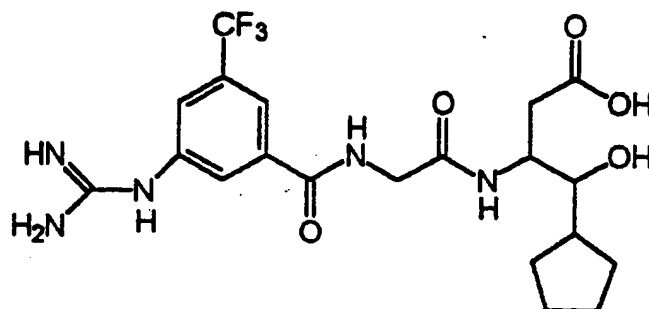
EXAMPLE 398

10 The above compound is prepared following substantially the procedure of Example 393, substituting ethynylmagnesium bromide for phenyl magnesium bromide in Step C.

EXAMPLE 399

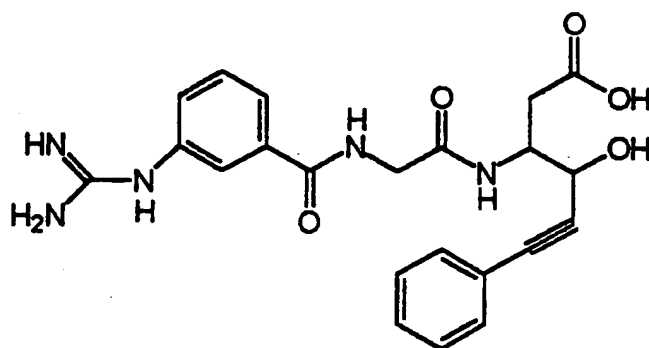
25 The above compound is prepared following substantially the procedure of Example 393, substituting allylmagnesium bromide for phenyl magnesium bromide in Step C.

- 632 -

EXAMPLE 400

10 The above compound is prepared following substantially the procedure of Example 393, substituting cyclopentylmagnesium bromide for phenyl magnesium bromide in Step C.

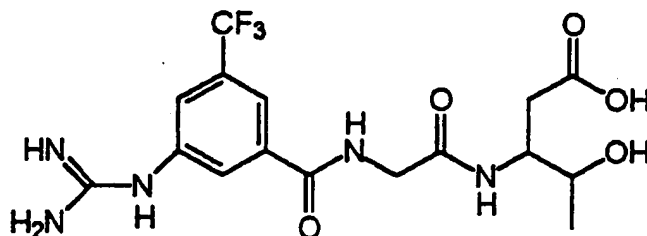
15 EXAMPLE 401



25 The above compound is prepared following substantially the procedure of Example 393, substituting phenylethynylmagnesium bromide for phenyl magnesium bromide in Step C.

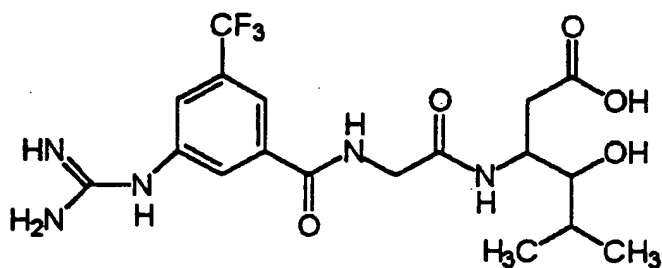
30

- 633 -

EXAMPLE 402

10 The above compound is prepared following substantially the procedure of Example 393, substituting methylmagnesium bromide for phenyl magnesium bromide in Step C.

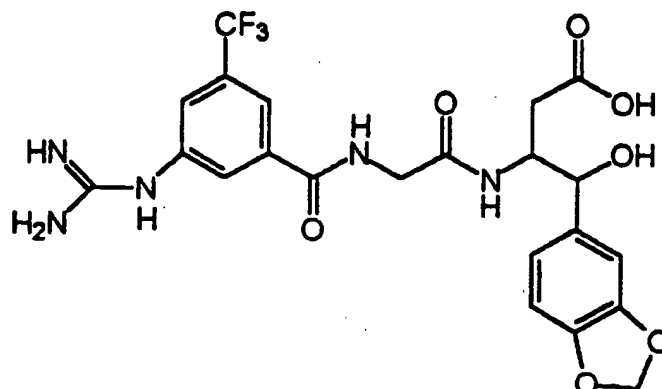
15 EXAMPLE 403



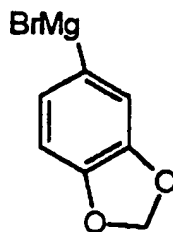
25 The above compound is prepared following substantially the procedure of Example 393, substituting isopropylmagnesium bromide for phenyl magnesium bromide in Step C.

30

- 634 -

EXAMPLE 404Step A

Preparation of 4-bromomagnesium-1,2-(methylenedioxy)benzene



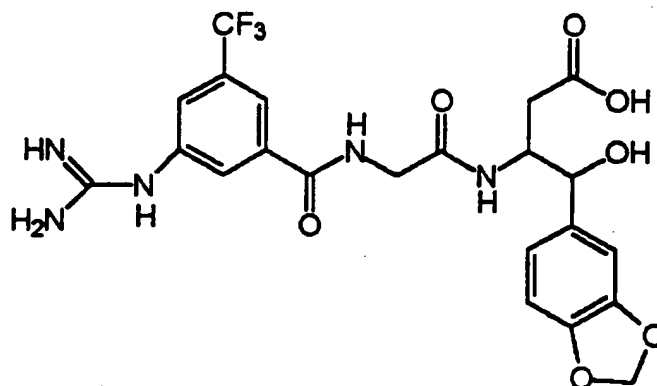
20

To 1.74 gm (0.072 mole) freshly-ground magnesium in 100 mL dry THF in a 250 mL round bottom flask was added in a dropwise fashion 13.1 gm (0.062 mole) 4-bromo-1,2-(methylenedioxy)benzene in 50 mL dry THF. The reaction mixture was sonicated during the addition and the reaction temperature maintained below 50°C by use of a water bath. Upon completion of reaction the mixture was filtered and used in the next step.

- 635 -

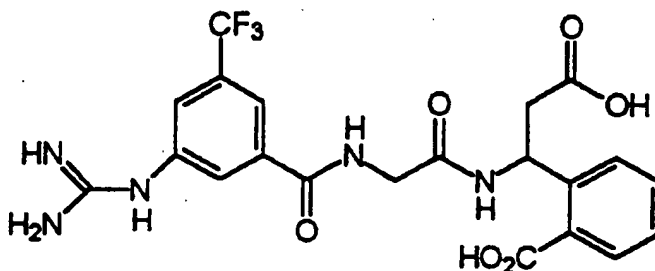
Step B

Preparation of

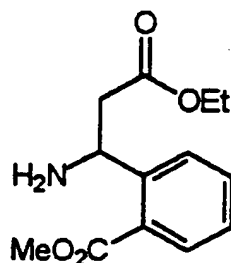


The above compound is prepared following substantially the procedure of Example 393, substituting the grignard of Step A for phenyl magnesium bromide in Example 393, Step C.

- 636 -

EXAMPLE 405Step A

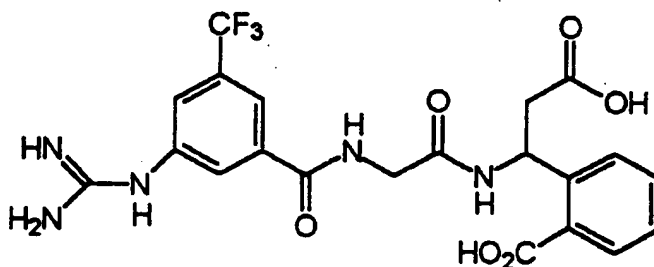
Preparation of



The above compound is prepared according to the procedure of Example 55, Step A, substituting methyl-2-formylbenzoate for 2-furancarboxaldehyde.

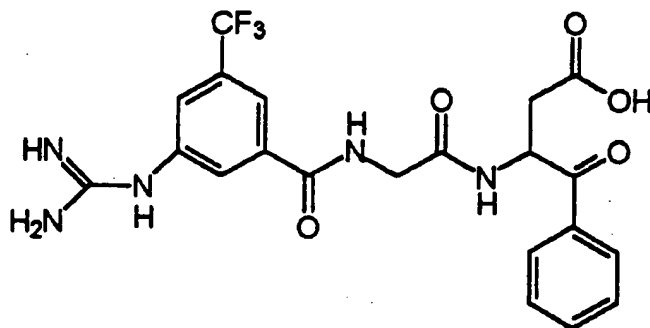
Step B

Preparation of

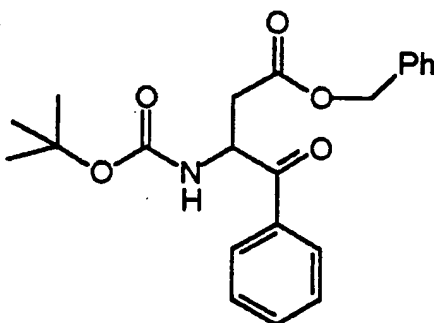


The above compound is prepared according to the procedure of Example 55, Steps B and C, substituting the product of Step A for the product of Example 55, Step A.

- 637 -

EXAMPLE 406Step A

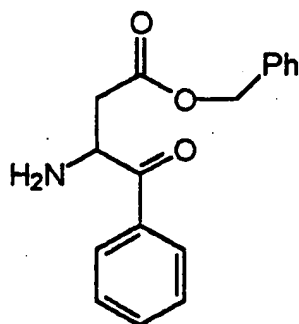
10 Preparation of



20 The product of Example 393, Step C is oxidized to the above ketone using the procedure of Example 393, Step B.

Step B

25 Preparation of

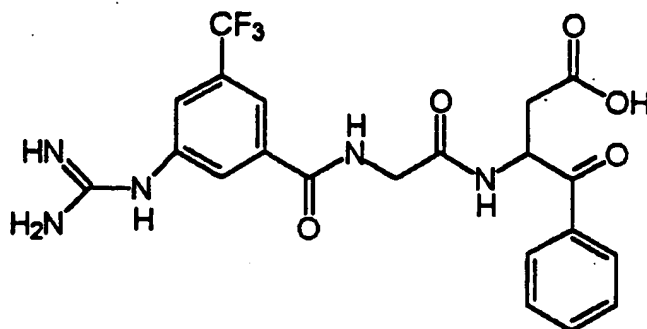


The above product is prepared using the procedure of Example 393, Step E using the product of Step A above.

- 638 -

Step C

Preparation of



The Example compound is prepared using substantially the procedure of Example 374, substituting the product of Step B for the compound prepared in Example 233, Step B. The desired product is obtained by converting the benzyl ester to the corresponding carboxylic acid by hydrolysis using substantially the procedure of Example 4 and isolating the desired product by C-18 RPHPLC.

- 639 -

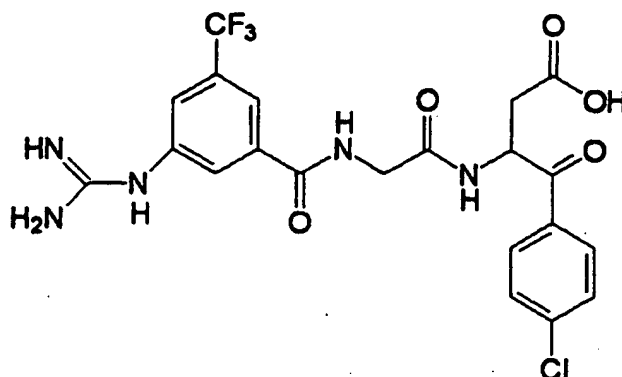
Example 407-414

Using the procedure of Example 406, substituting the appropriate protected aspartyl alcohols prepared in

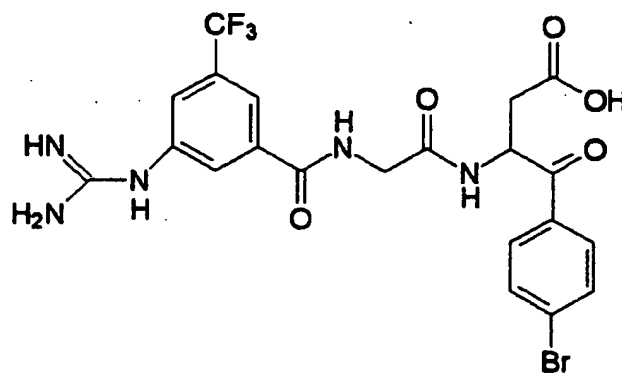
- 5 Examples 394-403 for the aspartyl alcohol of Example 406, Step A, the following representative compounds are prepared:

- 640 -

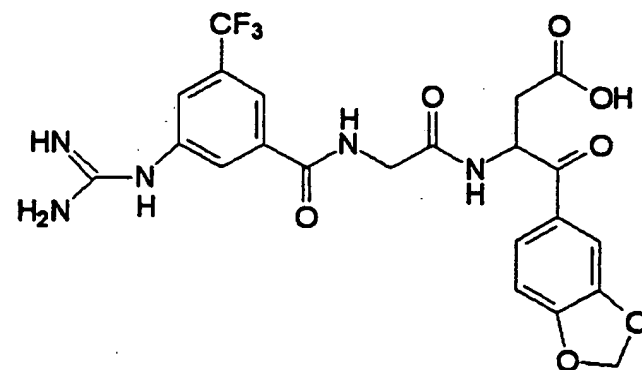
Ex. 407



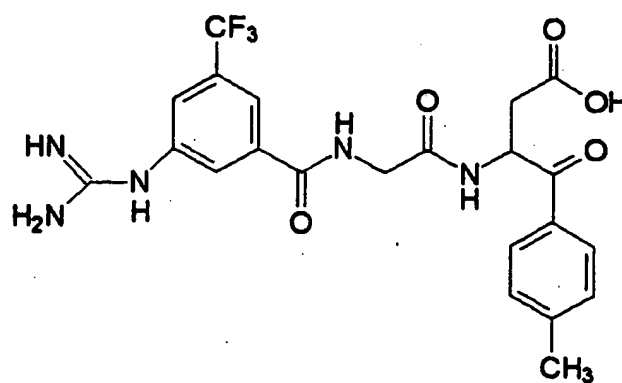
Ex. 408



Ex. 409

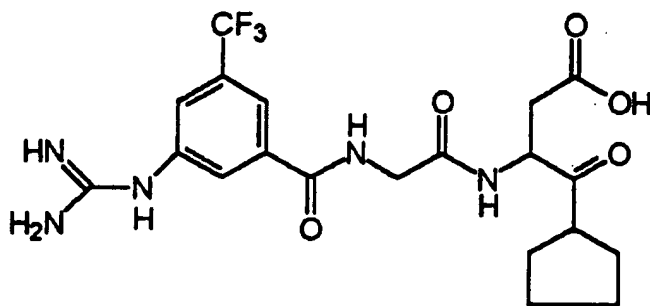


Ex. 410

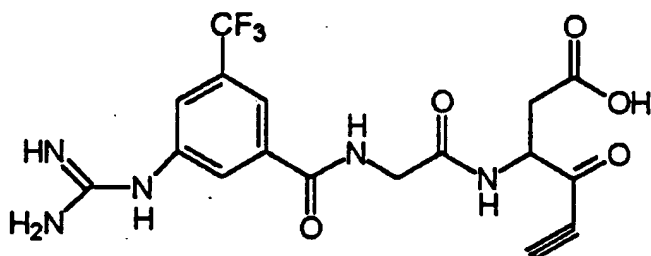


- 641 -

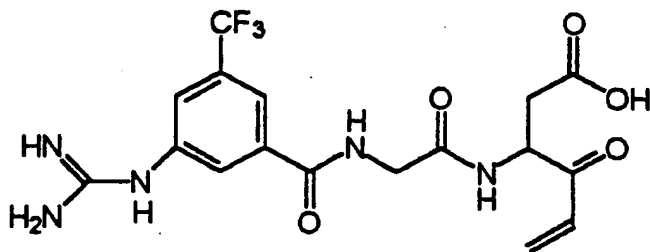
Ex. 411



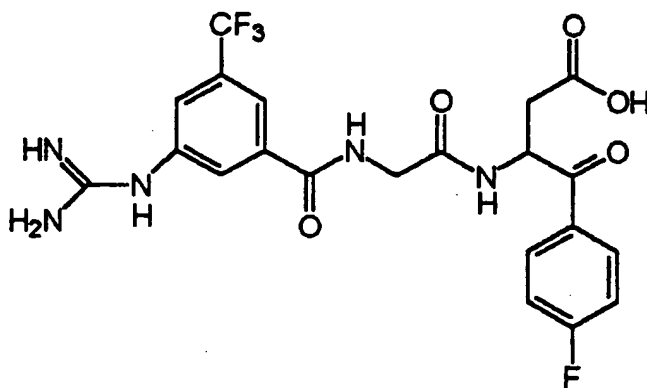
Ex. 412



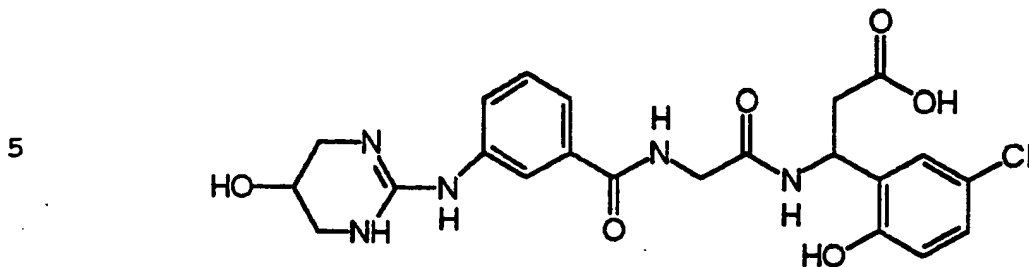
Ex. 413



Ex. 414

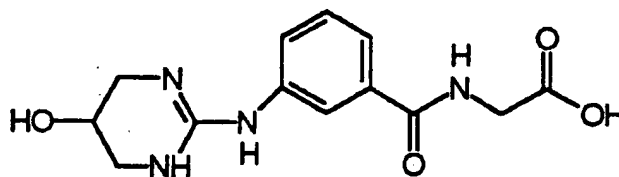


- 642 -

Example 415

Preparation of

10



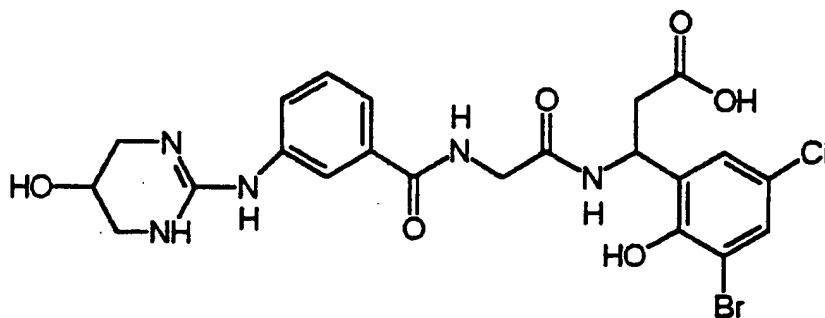
15 Step A

To the product of Example 23, Step A in DMF is added excess 1,3-diamino-2-hydroxypropane and catalytic DMAP and the solution heated until substantially complete conversion of the starting S-methylisothiuronium salt is achieved. The desired product may be isolated by precipitation of the zwitterion or by preparative C-18 RPHPLC (for a related procedure see U.S. Patent 2,899,426). After drying to remove water, the hydrochloride salt is formed by stirring the zwitterion in excess 4N HCl in dioxane (Aldrich) and isolating the HCl salt by filtration.

20

25

- 643 -

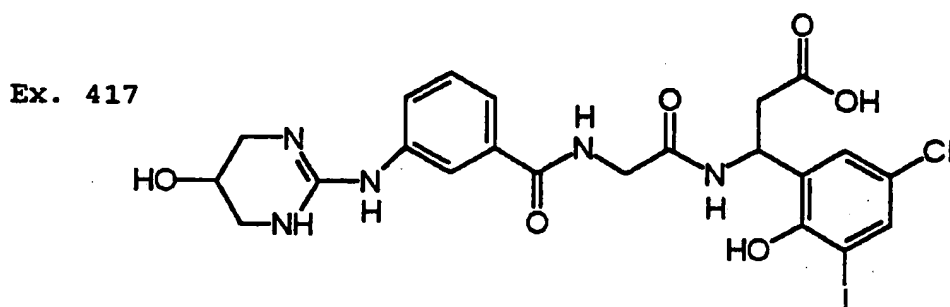
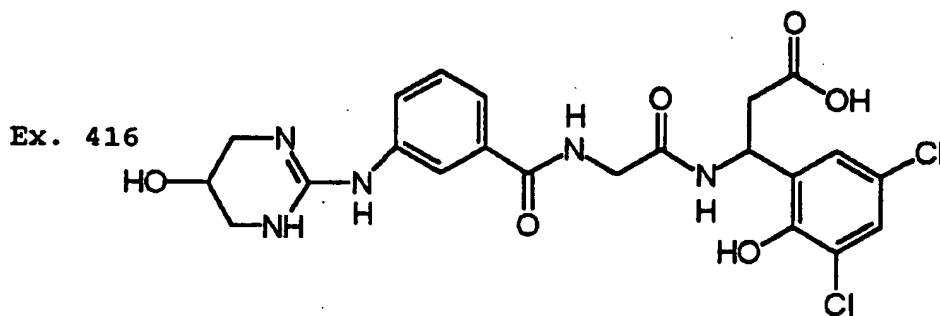
Step B

The above compound is prepared using substantially the procedure of Example 233, substituting the product of Step A for GHIA hydrochloride in Example 233, Step C.

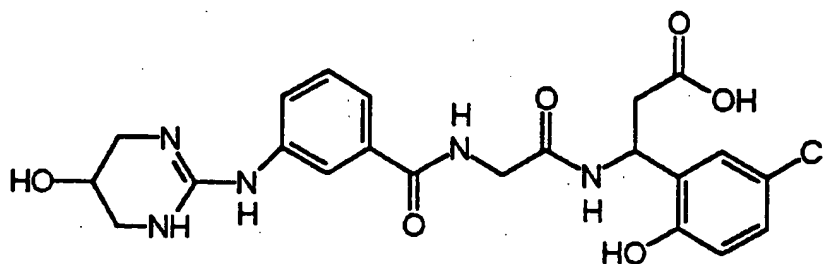
- 644 -

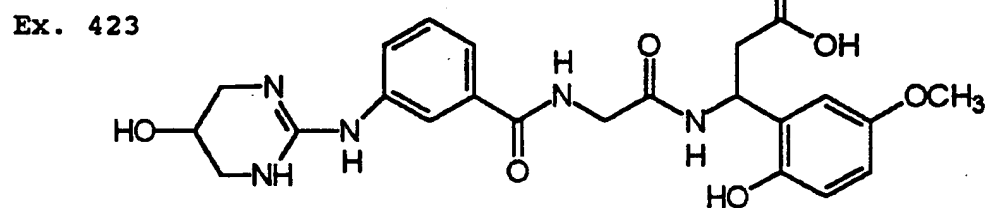
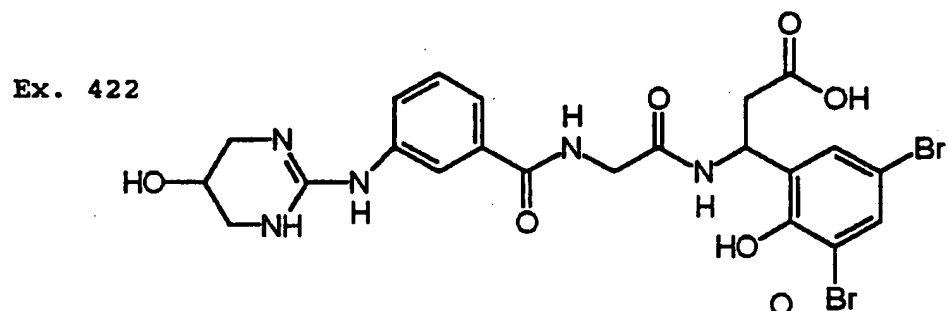
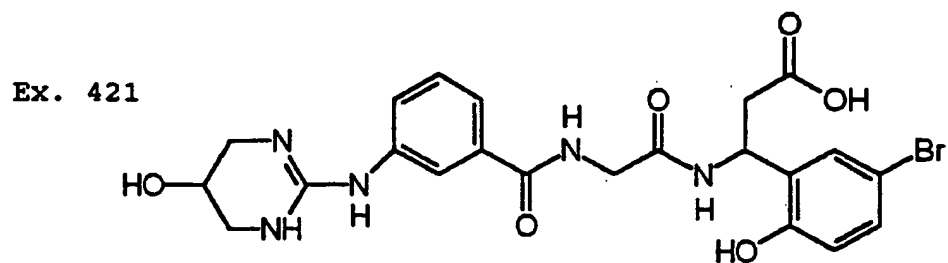
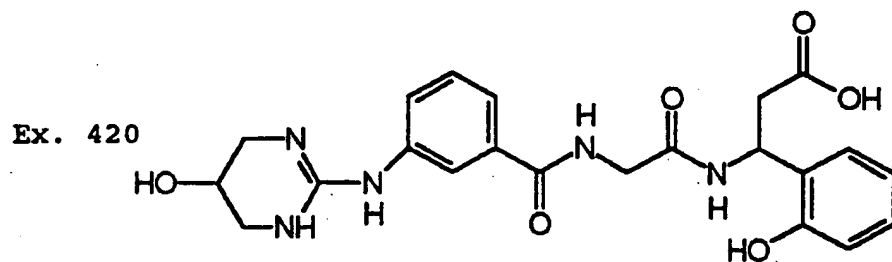
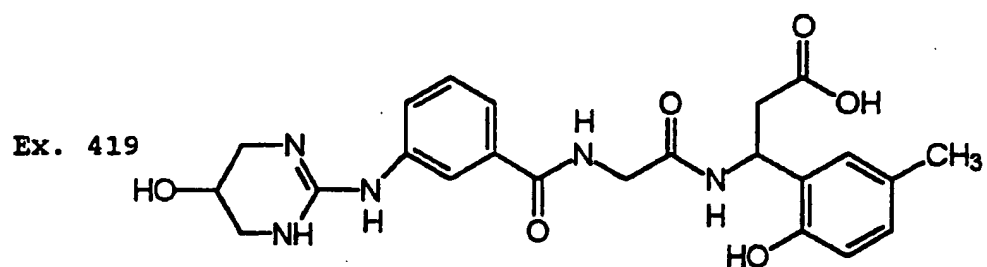
Example 416-439

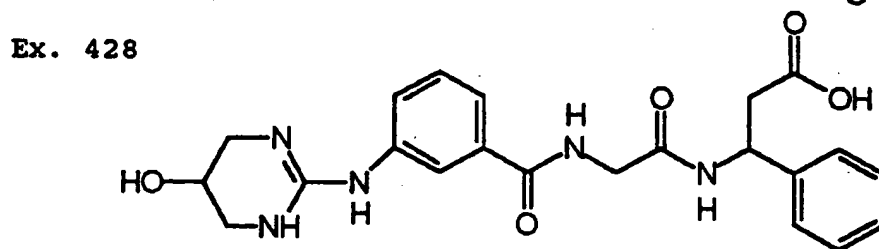
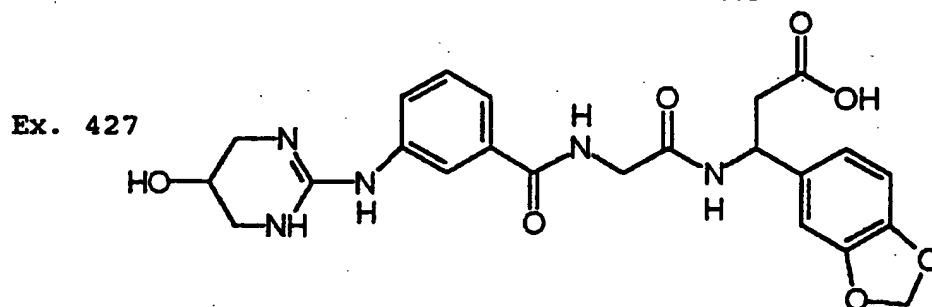
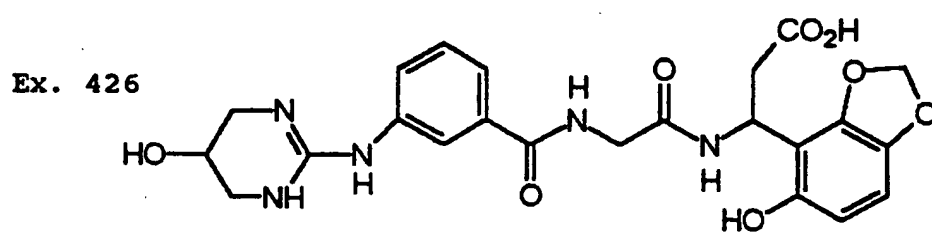
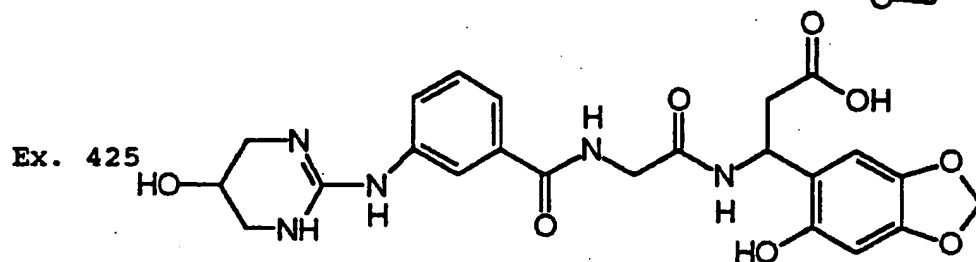
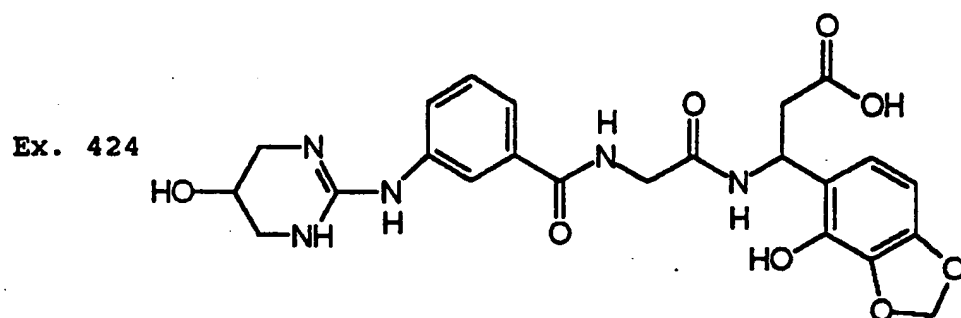
Using substantially the procedure of Example 415, substituting the appropriate amine for (RS)-4-amino-6-chloro-8-bromo-hydrocoumarin hydrochloride the following representative compounds may be prepared:

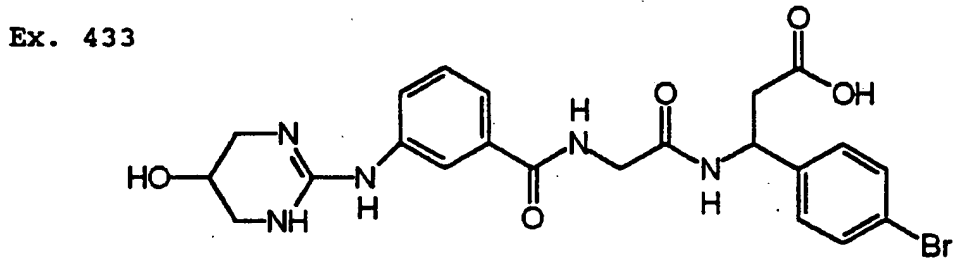
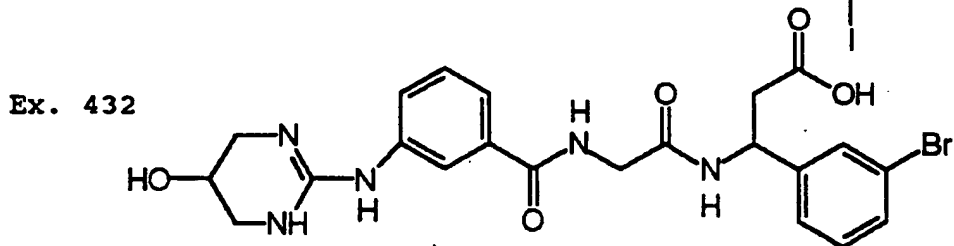
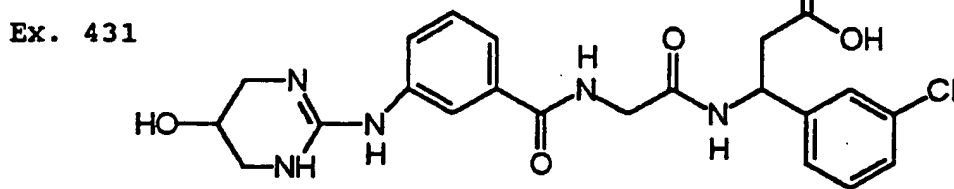
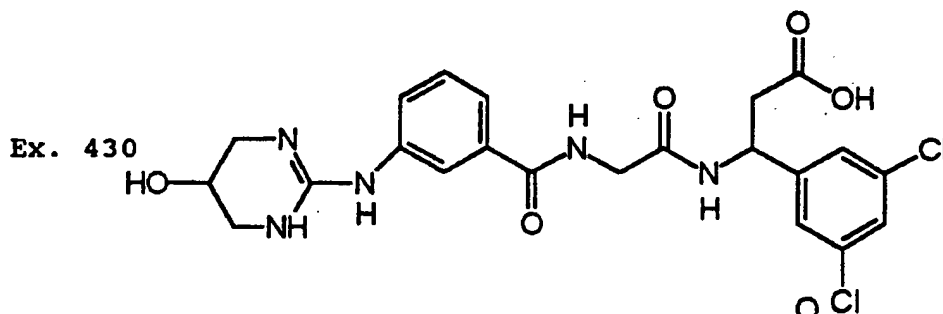
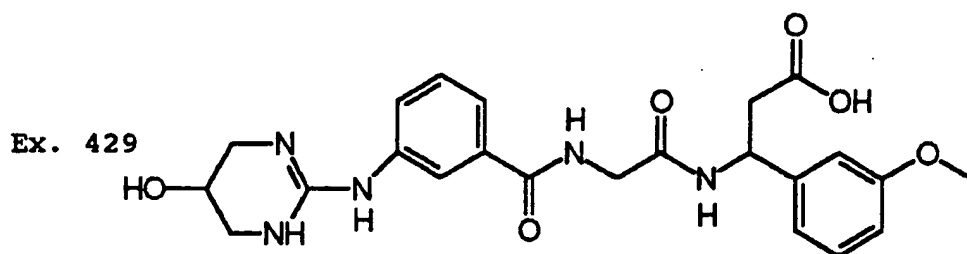


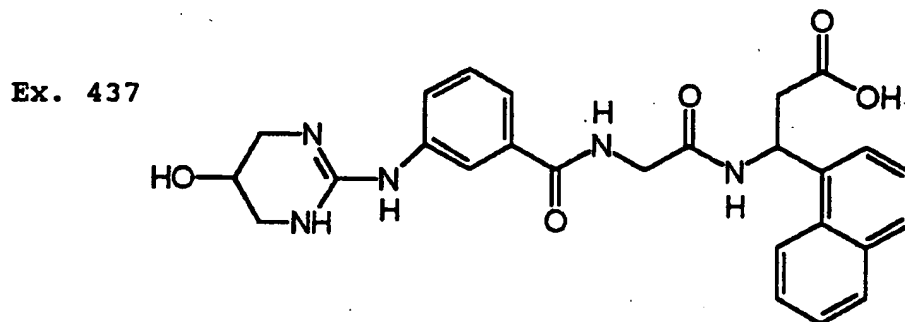
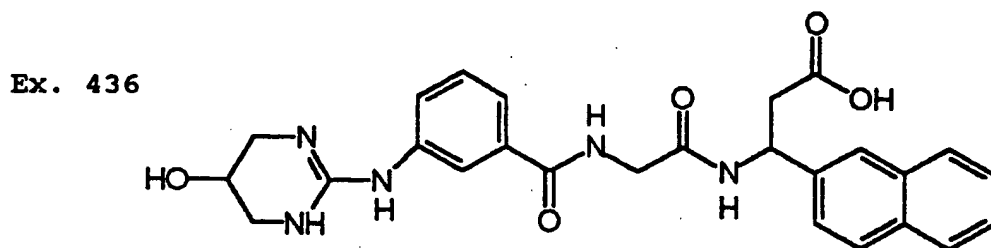
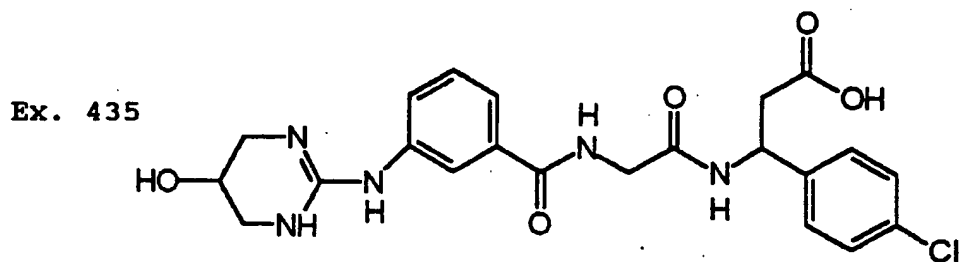
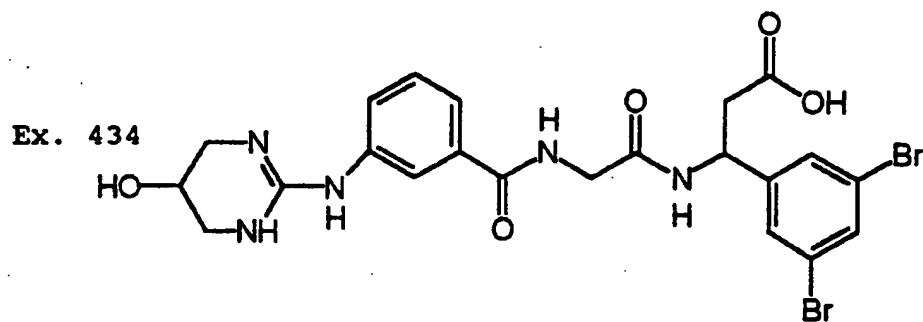
Ex. 418





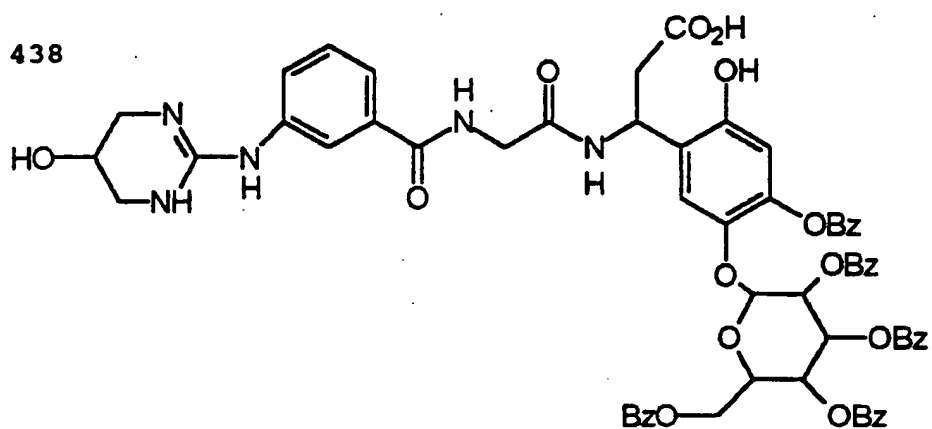




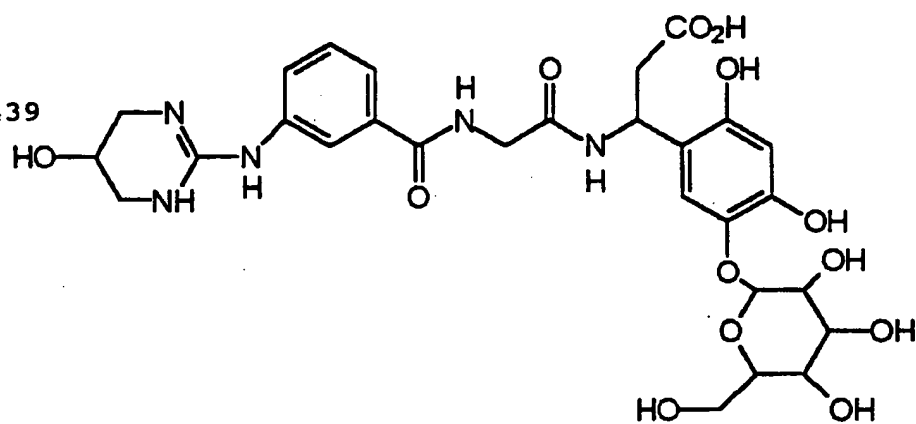


- 649 -

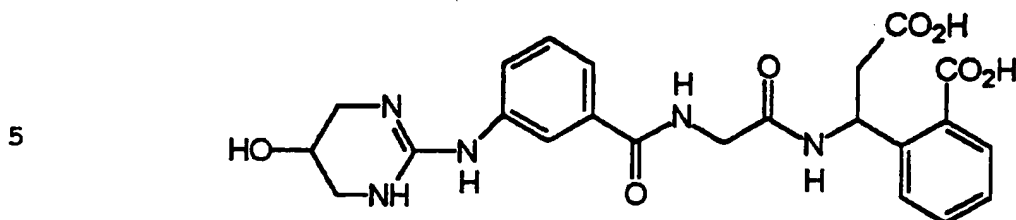
Ex. 438



Ex. 439

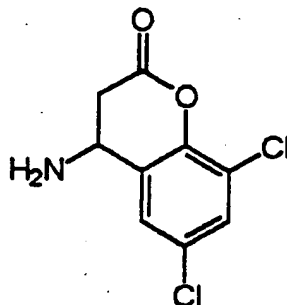


- 650 -

Example 440Step A

10

15

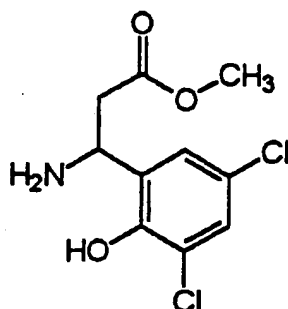


The above compound was prepared using the procedure of Example 233, Steps A and B, substituting 3,5-dichlorosalicylaldehyde for 3-bromo-5-chlorosalicylaldehyde in Step A. NMR and MS were consistent with the proposed structure (HCl salt).

Step B

25

30

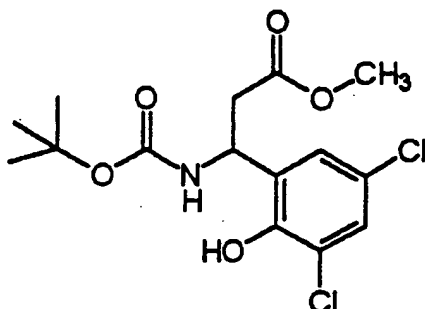


The above compound is prepared by treating the product of Step A with dry HCl gas in methanol in a

- 651 -

suitable reactor while maintaining vigorous stirring. Upon completion of reaction excess HCl is removed under vacuum and the solution concentrated to dryness. The crude product is used in the next step. Alternatively, the product may be isolated by C-18 RPHPLC and lyophilized to obtain substantially pure material.

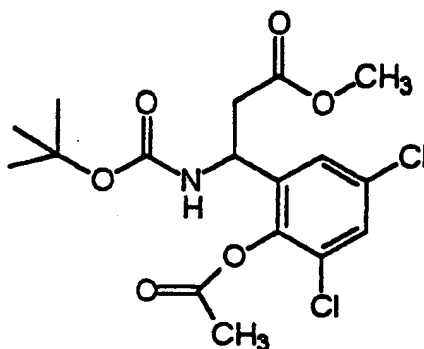
Step C



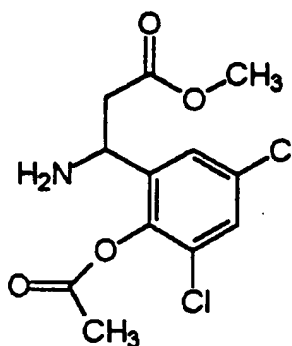
The above compound is prepared by taking the product of Step B and dissolving in DMF. To the stirred solution is added an equimolar amount of both di-tert butyl dicarbonate and triethylamine with a catalytic amount of DMAP. Upon completion of the reaction volatiles are removed under vacuum and the product partitioned between dilute aqueous hydrochloric acid and ethyl acetate. The organic layer is washed with water, dried (Na_2SO_4) and concentrated to provide substantially the above compound that may be employed in the next step without further purification. Alternatively, the product may be isolated by C-18 RPHPLC and lyophilized to obtain substantially pure material.

30

- 652 -

Step D

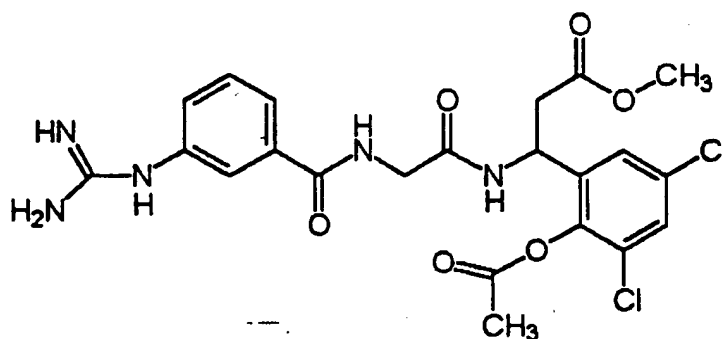
The above compound is prepared by adding under an inert atmosphere an equivalent of acetic anhydride or acetyl chloride and an equivalent of triethylamine to a stirred solution of the product from Step C in DMF. Upon completion of reaction volatiles are removed under vacuum and the reaction residue partitioned between dilute aqueous hydrochloric acid and ethyl acetate. The organic layer is washed with aqueous sodium bicarbonate, dried (Na_2SO_4) and concentrated to provide substantially the above compound that may be employed in the next step without further purification. Alternatively, the product may be isolated by C-18 RPHPLC and lyophilized to obtain substantially pure material.

Step E

- 653 -

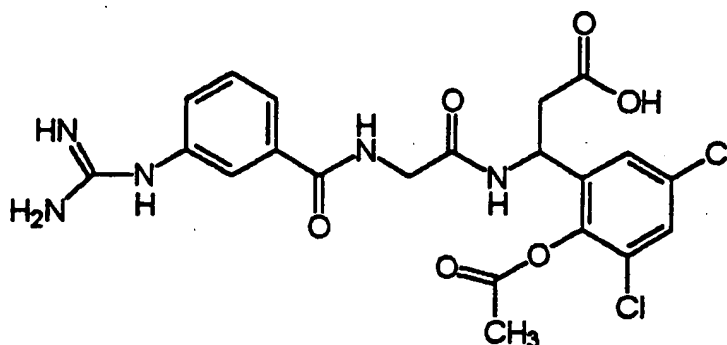
The above compound is prepared by treating the product of Step D with 4 N HCl in dioxane with vigorous stirring. Shortly after cessation of gas evolution excess HCl gas is removed *in vacuo* and the reaction mixture concentrated at less than about 40°C. The product is trituated with diethyl ether to obtain substantially the desired product. Alternatively, the product may be isolated by C-18 RPHPLC and lyophilized to obtain substantially pure mater.

Step F

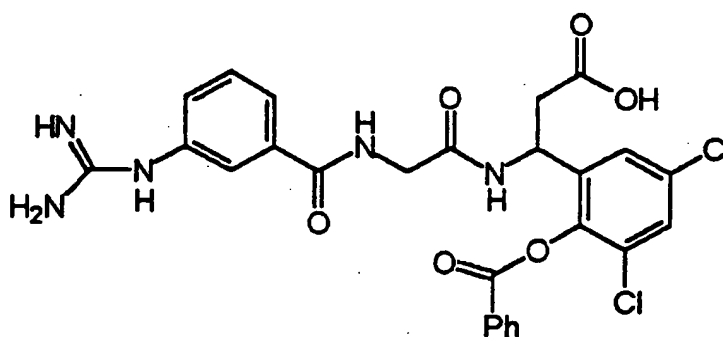


The above compound is prepared according to the procedure of Example 230, Step B, substituting the product of Step E for the product of Example 230, Step A.

- 654 -

Example 441

The above compound is prepared by treating a DMF mixture of the compound of Example 225 with two equivalents of N-methylmorpholine and one equivalent of acetic anhydride or acetyl chloride. Upon completion of the reaction the desired product may be isolated by C-18 RPHPLC and lyophilization.

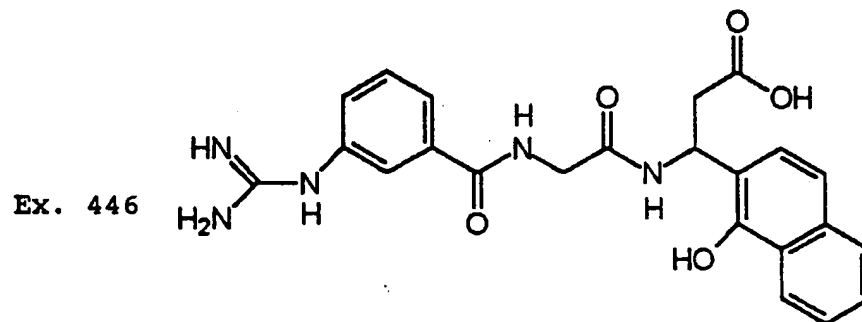
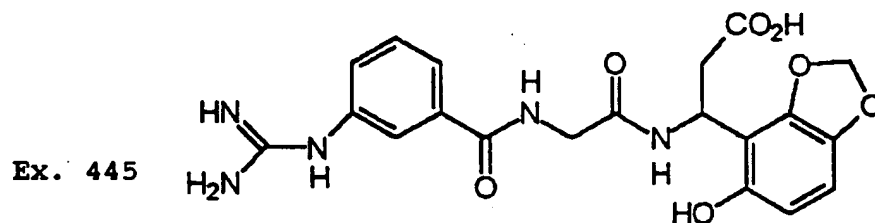
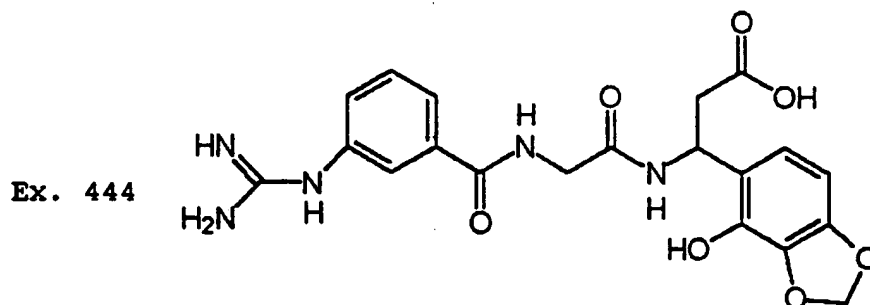
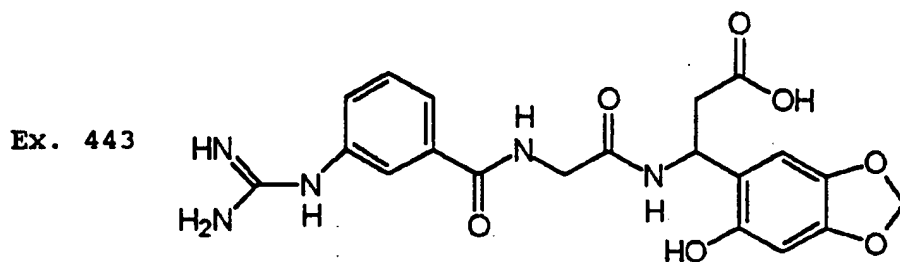
Example 442

The above compound is prepared by treating a DMF mixture of the compound of Example 225 with two equivalents of N-methylmorpholine and one equivalent of benzoic anhydride or benzoyl chloride. Upon completion of the reaction the desired product may be isolated by C-18 RPHPLC and lyophilization.

- 655 -

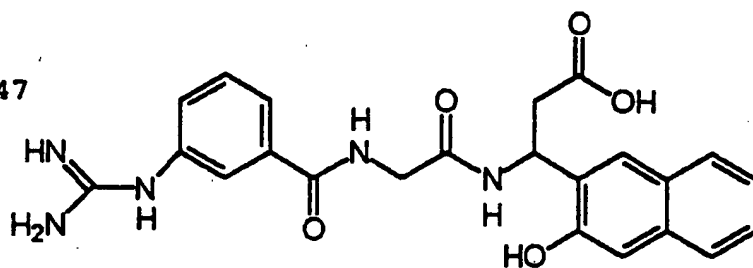
Example 443-452

Using substantially the procedure of Example 230, Step B and substituting the appropriate amine for the product of Example 230, Step A, the following
5 representative compounds may be prepared:

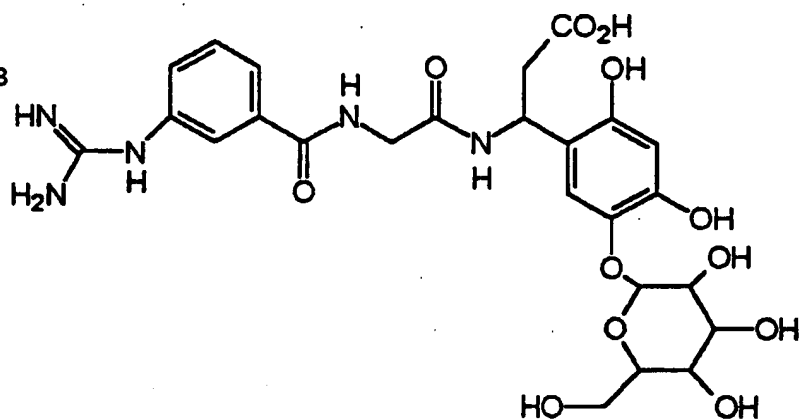


- 656 -

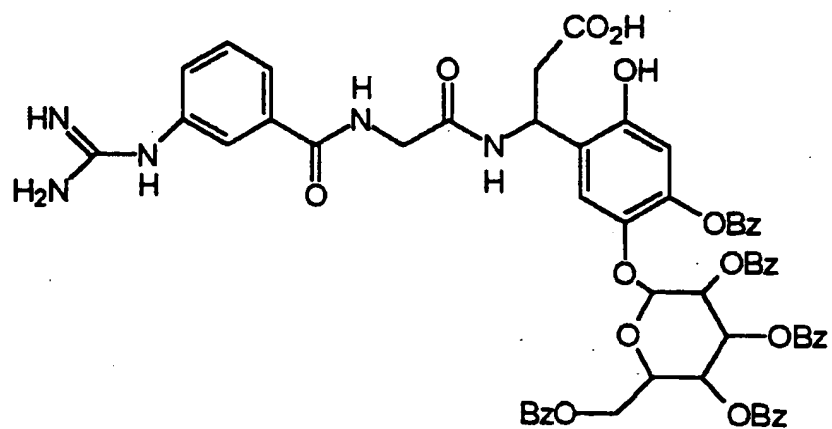
Ex. 447



Ex. 448

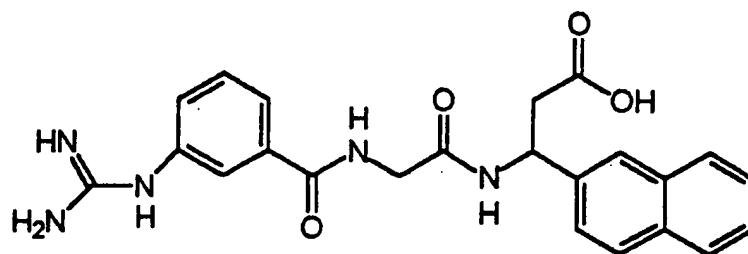


Ex. 449

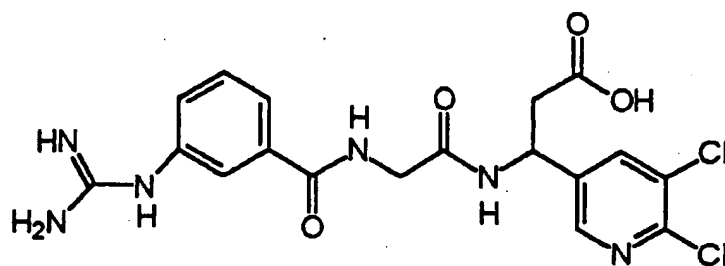


- 657 -

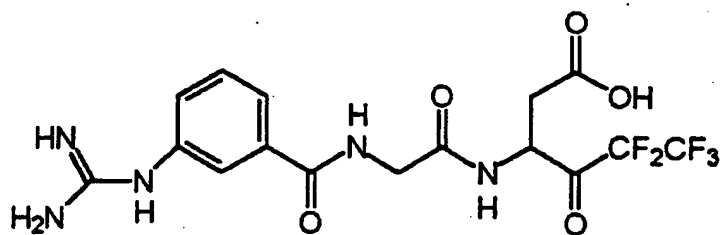
Ex. 450



Ex. 451



Ex. 452

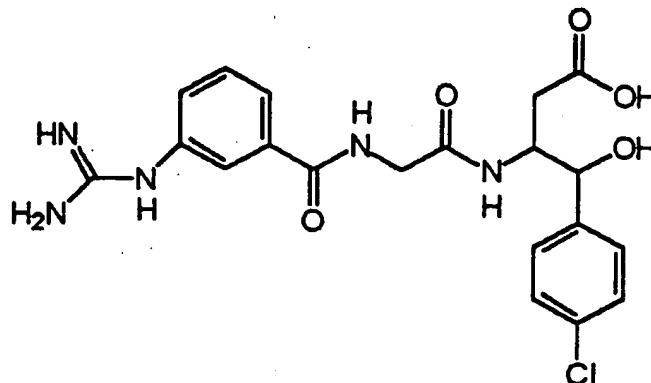


- 658 -

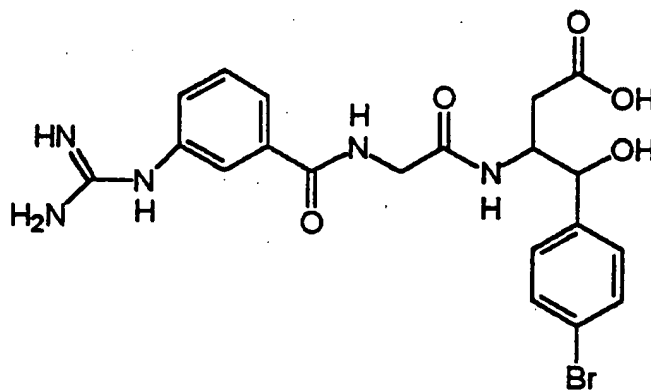
Example 453-460

Using the procedur of Example 393, substituting the appropriate amine hydrochloride for the product of Step E in Step F and substituting GIHA HCl for 3-guanidino-5-trifluoromethylhippuric acid in Step F the following representative compounds may be prepared:

Ex. 453

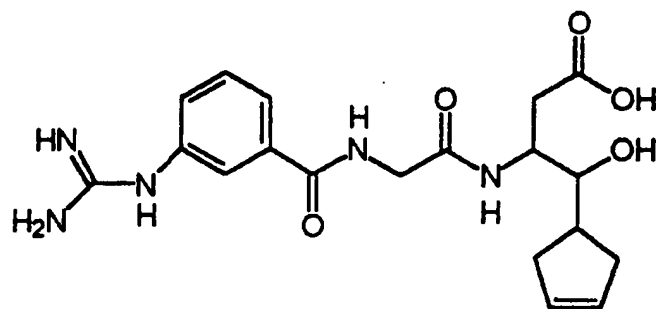


Ex. 454

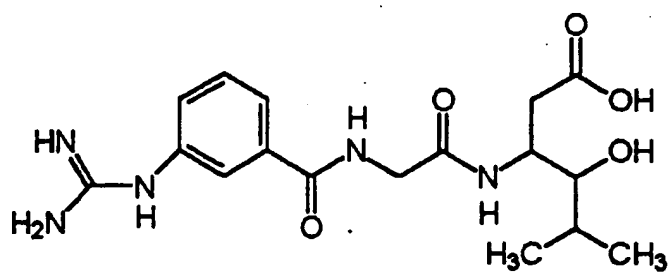


- 659 -

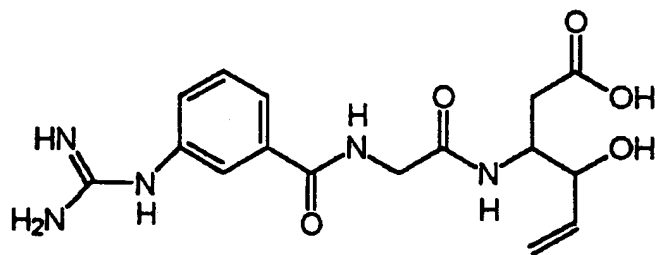
Ex. 455



Ex. 456

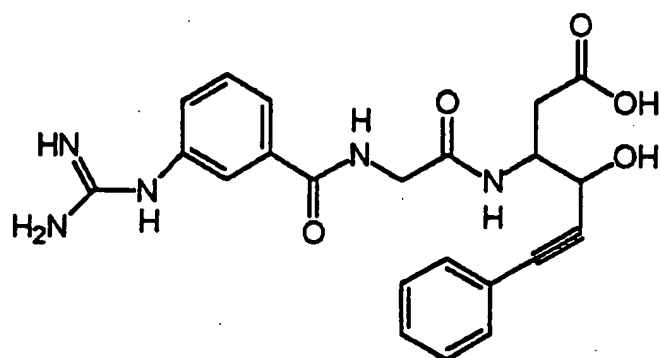


Ex. 457

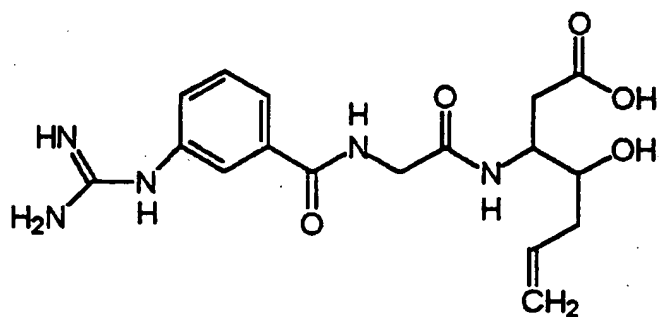


- 660 -

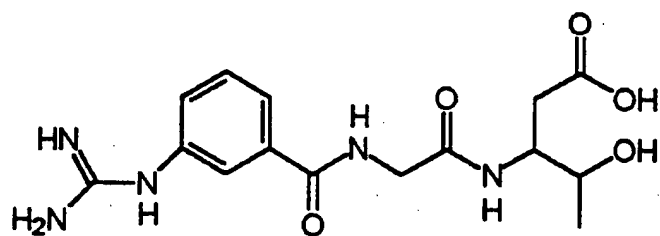
Ex. 458



Ex. 459



Ex. 460

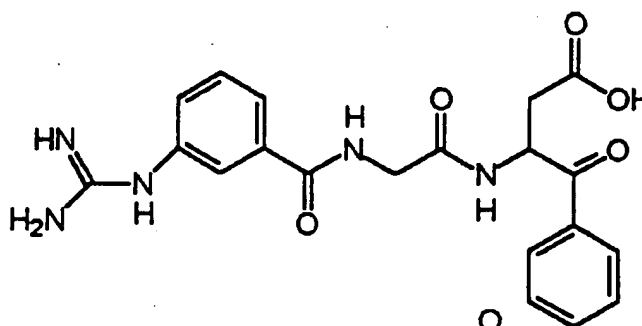


- 661 -

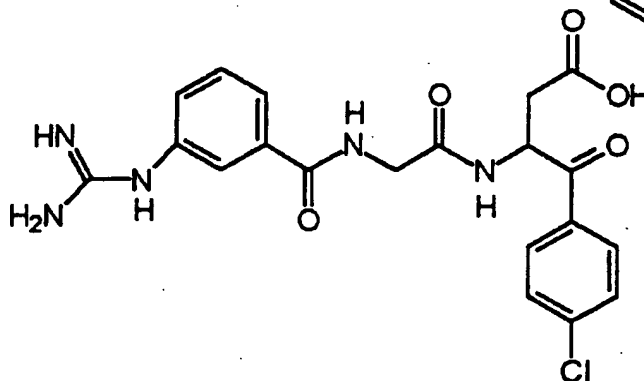
Example 461

Using the procedure of Example 406, substituting the appropriate protected aspartyl alcohol prepared in Examples 394-403 for the aspartyl alcohol of Example 406, Step A, and substituting GIHA HCl for 3-guanidino-5-trifluoromethylhippuric acid in Example 393, Step F the following representative compounds may be prepared:

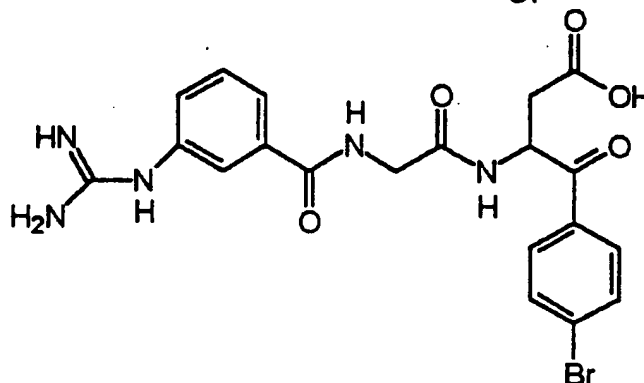
Ex. 461



Ex. 462

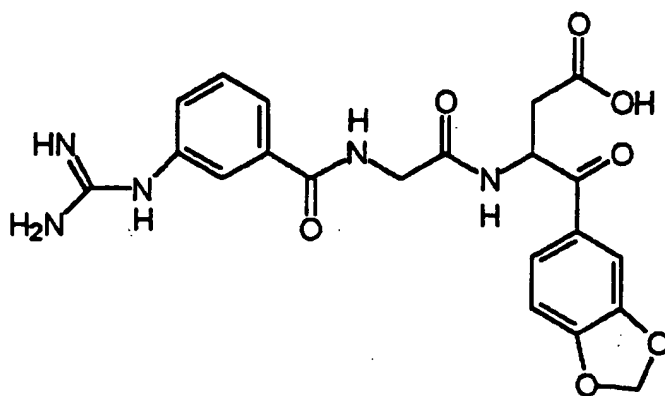


Ex. 463

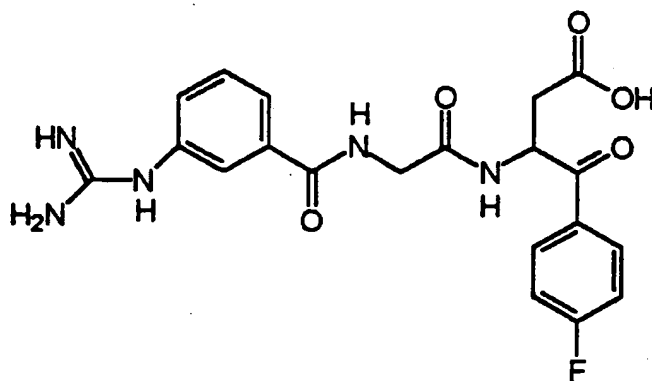


- 662 -

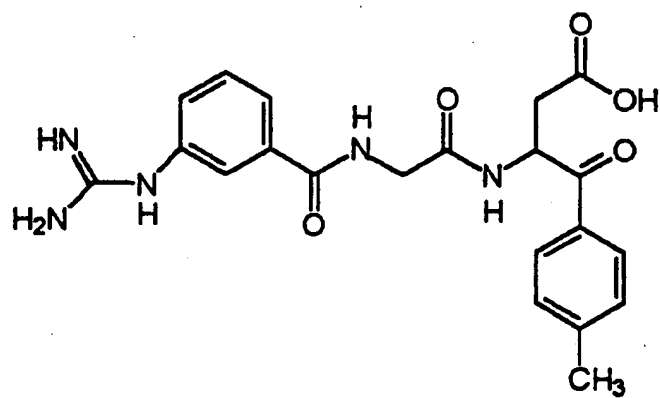
Ex. 464



Ex. 465

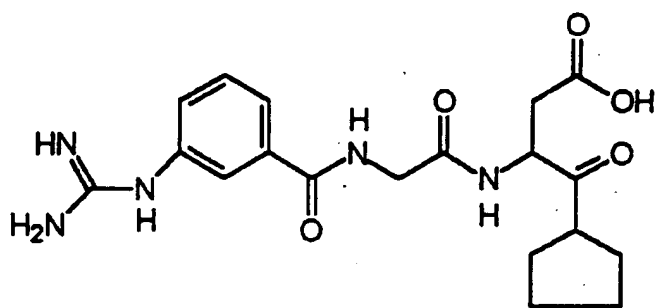


Ex. 466

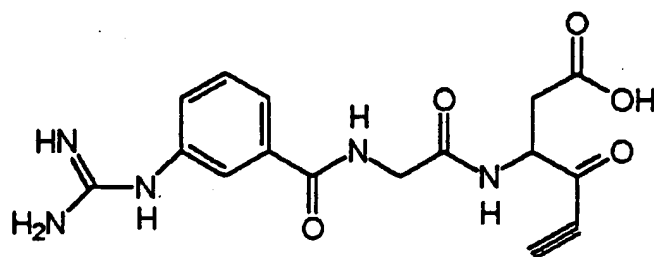


- 663 -

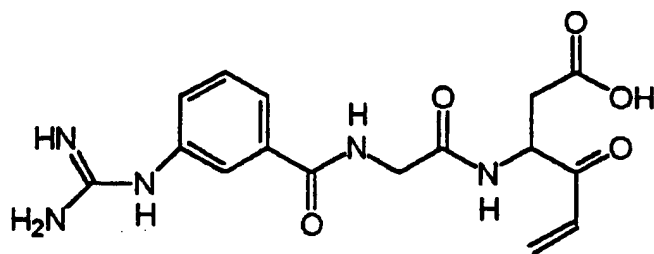
Ex. 467



Ex. 468



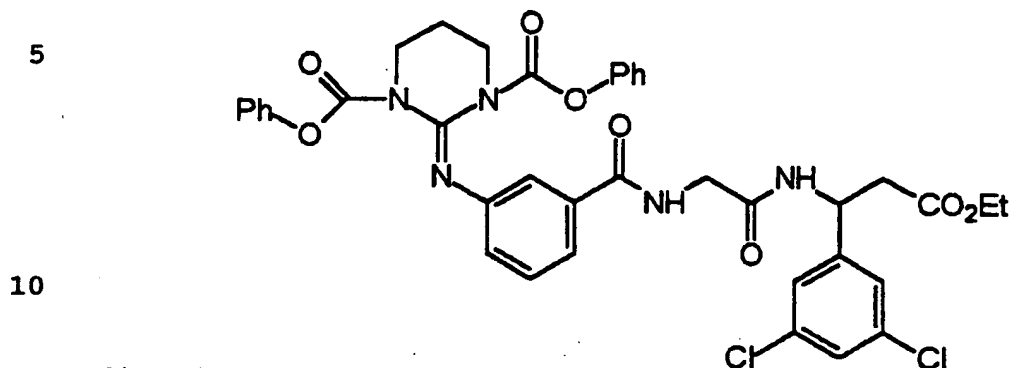
Ex. 469



- 664 -

Example 470

Preparation of

Step A

To 3,4,5,6-tetrahydro-2-pyrimidinethiol (Aldrich) (5.0 g, 0.043 mole) and triethylamine (8.7 g, 0.086 mole) in CH_2Cl_2 (50 mL) was added dropwise and at ice bath temperature, phenylchloroformate [(Aldrich) 13.5 g, 0.086 mole)]. The reaction was then stirred overnight at room temperature. The precipitate was filtered and washed with CH_2Cl_2 . The CH_2Cl_2 filtrate was washed with H_2O (3X), dried over MgSO_4 and removed under vacuum. The residue was recrystallized from 50% EtOAc/Hexane to yield 9.03 g of 3,4,5,6-tetrahydro-2-pyrimidinethione-N,N'-diphenylcarbamate as a yellow solid.

MS and NMR are consistent with the desired structure.

Step B

To the product from Example 282, Step C (200 mg, 0.00042 mole), the product from Step A above (150 mg, 0.00042 mole) and triethylamine (142 mg, 0.0014 mole) in 3 mL DMF was added 250 mg (0.00046 mole) HgCl_2 at ice bath temperature. The reaction was stirred at ice bath temperature for $\frac{1}{2}$ hour and at room temperature for 2 hours. 100 mg additional HgCl_2 was added and the reaction was stirred overnight at 60°C . Excess ethyl acetate was added and the slurry was filtered through

- 665 -

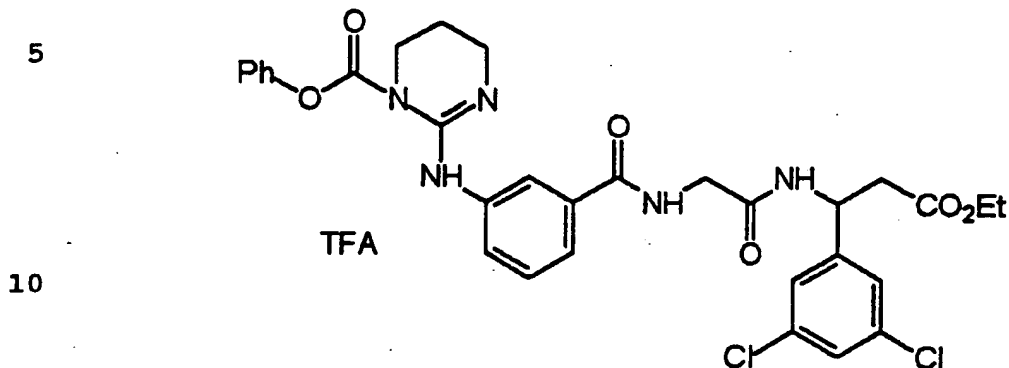
celite. The filtrate was wash d with H₂O (3X), passed through a pad of silica gel and th product isolated by silica gel chromatography to yield the above compound (110 mg) as a white solid.

5. MS and NMR were consistent with the desired structure.

- 666 -

Example 471

Preparation of

Step A

15 To 3,4,5,6-tetrahydro-2-pyrimidinethiol (Aldrich) (10 g, 0.086 mole) in absolute ethanol (75 mL) is added methyl iodide (12.2 g, 0.086 mole). The reaction was stirred at reflux for 2.5 hours. The solvent was removed under vacuum and the residue dried to yield

20 3,4,5,6-tetrahydro-2-methylthiopyrimidine·HI (22 g) as a white solid.

MS and NMR were consistent with the desired structure.

25 Step B

To the product from Step A above (5.16 g, 0.02 mole) and triethylamine (4.1 g, 0.04 mole) in CH_2Cl_2 (25 mL) was added phenylchloroformate (Aldrich) (3.13 g, 0.02 mole) dropwise at ice bath temperature. The

30 reaction was then stirred overnight at room temperature. The precipitate was filtered and washed with CH_2Cl_2 . The CH_2Cl_2 from the filtrate was washed with H_2O (3X), dried over MgSO_4 and removed under vacuum to yield 3,4,5,6-tetrahydro-2-methylthiopyrimidine-N-phenylcarbamate (4.8 g) as a white solid.

35

MS and NMR were consistent with the desired structure.

- 667 -

Step C

To the product from Step B above (2 g, 0.008 mol) in CH₂CN (12 mL) was added the product of Example M, Step B (1.84 g, 0.008 mole). The reaction was stirred at reflux overnight and the product isolated by RPHPLC to yield 3,4,5,6-tetrahydro-N-phenylcarbamyl-2-pyrimidine-m-aminohippuric acid·TFA (1 g) as a white solid.

10 Step D

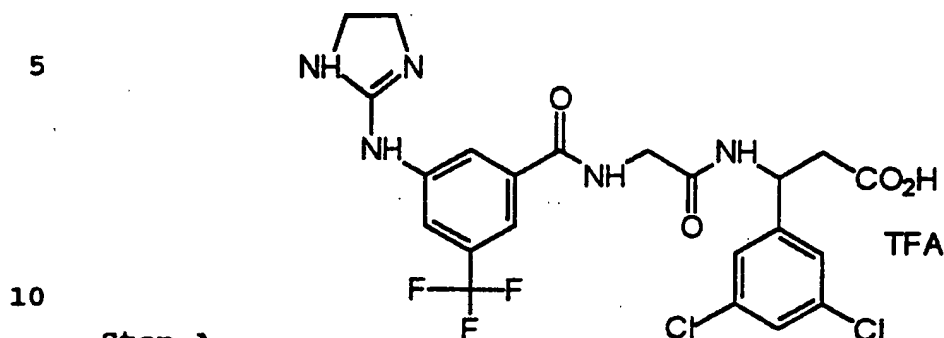
The above compound was prepared according to the methodology of Example 174, substituting an equivalent amount of 3,5-dichlorobenzaldehyde for 3,4-dichlorobenzaldehyde in Example 174, Step A and substituting an equivalent amount of the product from Step C above for m-guanidinohippuric acid·HCl in Example 174, Step B.

MS and NMR were consistent with the desired structure.

- 668 -

Example 472

Preparation of

Step A

To 2-methylthio-2-imidazoline·HI (Aldrich) (10 g, 0.041 mole) and triethylamine (4.14 g, 0.041 mole) in CH_2Cl_2 (50 mL) was added BOC anhydride (Aldrich) (8.94 g, 0.041 mole) at ice bath temperature. The reaction was stirred overnight at room temperature. The CH_2Cl_2 was washed with H_2O (3 X), dried over MgSO_4 , washed with H_2O (3 X), dried over MgSO_4 and removed under vacuum to yield N-BOC-2-methylthio-2-imidazoline (8.1 g) as a clear liquid which turned to a white solid upon standing.

MS and NMR were consistent with the desired structure.

Step B

To the product of Step A above (2.7 g, 0.0124 mole) in CH_3CN (6 mL) was added 3-amino-5-trifluoromethylbenzoic acid (synthesized by catalytic hydrogenation (Pd/C) of 3-nitro-5-trifluorobenzoic acid (Lancaster) followed by treatment with HCl) (3 g, 0.0124 mole). The reaction was stirred at 35-40°C for 10 days. After cooling to room temperature, the precipitate was filtered, washed with CH_3CN and dried to yield 3-(N-BOC-4,5-dihydroimidazol-2-yl)amino-5-trifluoromethylbenzoic acid HCl (3.2 g) as a white solid.

- 669 -

MS and NMR were consistent with the desired structure.

Step C

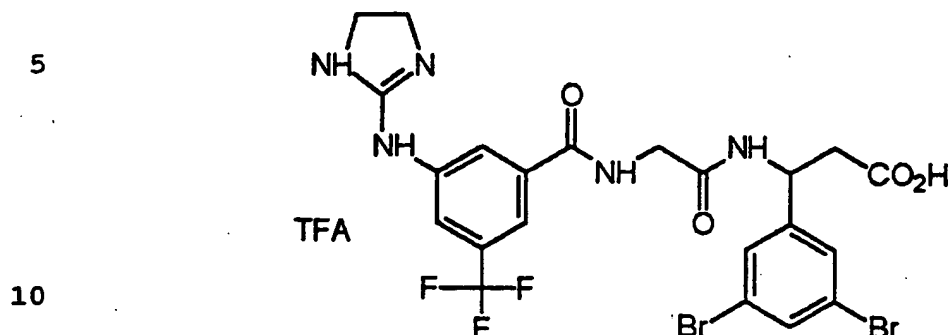
- 5 The above compound was prepared according to the methodology of Example 200, substituting an equivalent amount of the product from Step B above for the product from Step A in Example 199, Step B and by additionally treating the intermediate ethyl ester, N-BOC derivative
- 10 with TFA for 1 hour to remove the BOC protecting group.

MS and NMR were consistent with the desired structure.

- 670 -

Example 473

Preparation of

Step A

To 3-amino-5-trifluoromethylhippuric acid hydrochloride [prepared according to Example M, Steps A and B substituting 3-nitro-5-trifluoromethylbenzoyl chloride (prepared from 3-nitro-5-trifluoromethylbenzoic acid (Lancaster) and thionyl chloride for *m*-nitrobenzoyl chloride in Example M, Step A] (3 g, 0.01 mole) in CH₃CN (5 mL) was added the product from Example 472, Step A (2.2 g, 0.01 mole). The reaction was stirred at 35°C for 3 days then at reflux for 4 hours. After cooling, the CH₃CN was decanted off, the residue slurried several times in ether (ether decanted off) and then dried to yield 3-(4,5-dihydro-1H-imidazol-2-yl)amino-5-trifluoromethylhippuric acid·HCl (2.5 g) as a white solid.

MS and NMR were consistent with the desired structure.

Step B

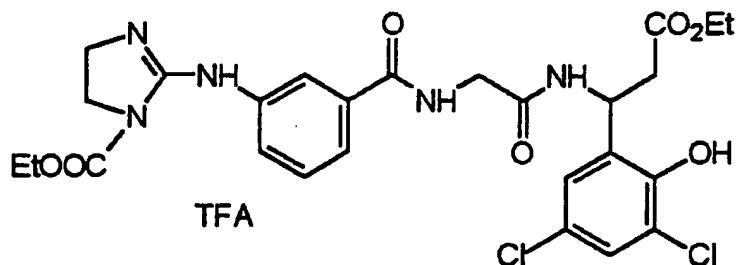
The above compound was prepared according to the methodology of Example 210, substituting an equivalent amount of the product from Step A above for *m*-guanidinohippuric acid·HCl in Example 174, Step B.

MS and NMR were consistent with the desired structure.

- 671 -

Example 474

Preparation of

Step A

To 2-methylthio-2-imidazoline·HI (Aldrich) (10 g, 0.041 mole) and triethylamine (8.3 g, 0.0082 mole) in CH_2Cl_2 (50 mL) was added ethylchloroformate (Aldrich) (4.5 g, 0.041 mole) dropwise at ice bath temperature. The reaction was stirred overnight at room temperature. The precipitate was filtered and washed with CH_2Cl_2 . The CH_2Cl_2 from the filtrate was washed with H_2O (3X), dried over MgSO_4 and removed under vacuum to yield 2-methylthio-2-imidazoline-N-ethylcarbamate (7.1 g) as a clear yellow oil.

MS and NMR were consistent with the desired structure.

Step B

To the product from Step A above (5.73 g, 0.0305 mole) in CH_3CN (12 mL) was added m-aminohippuric acid·HCl (Example M, Step B) (7.02 g, 0.0305 mole). The reaction was stirred overnight at room temperature then at 50°C for 6 hours and at 80°C for 2 hours. After cooling to room temperature and stirring at room temperature overnight, the precipitate was filtered, washed with CH_3CN and dried to yield 3-(4,5-dihydro-N-ethylcarbamate-imidazol-2-yl)aminohippuric acid·HCl (9.6 g) as a white solid.

MS and NMR were consistent with the desired structure.

- 672 -

Step C

The above compound was prepared according to the methodology of Example 174, substituting an equivalent amount of the product from Step B above for

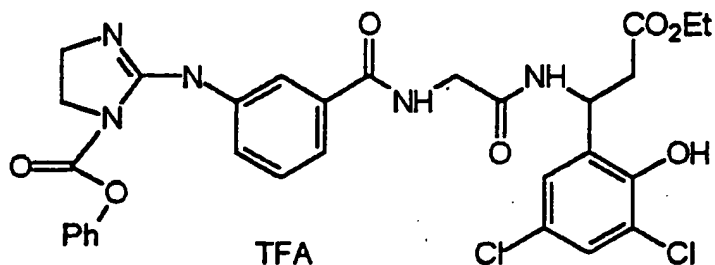
- 5 m-aminohippuric acid in Example 174, Step B and an equivalent amount of the product from Example 230, Step A for the product from Example 174, Step A in Example 174, Step B.

10 MS and NMR were consistent with the desired structure.

- 673 -

Example 475

Preparation of



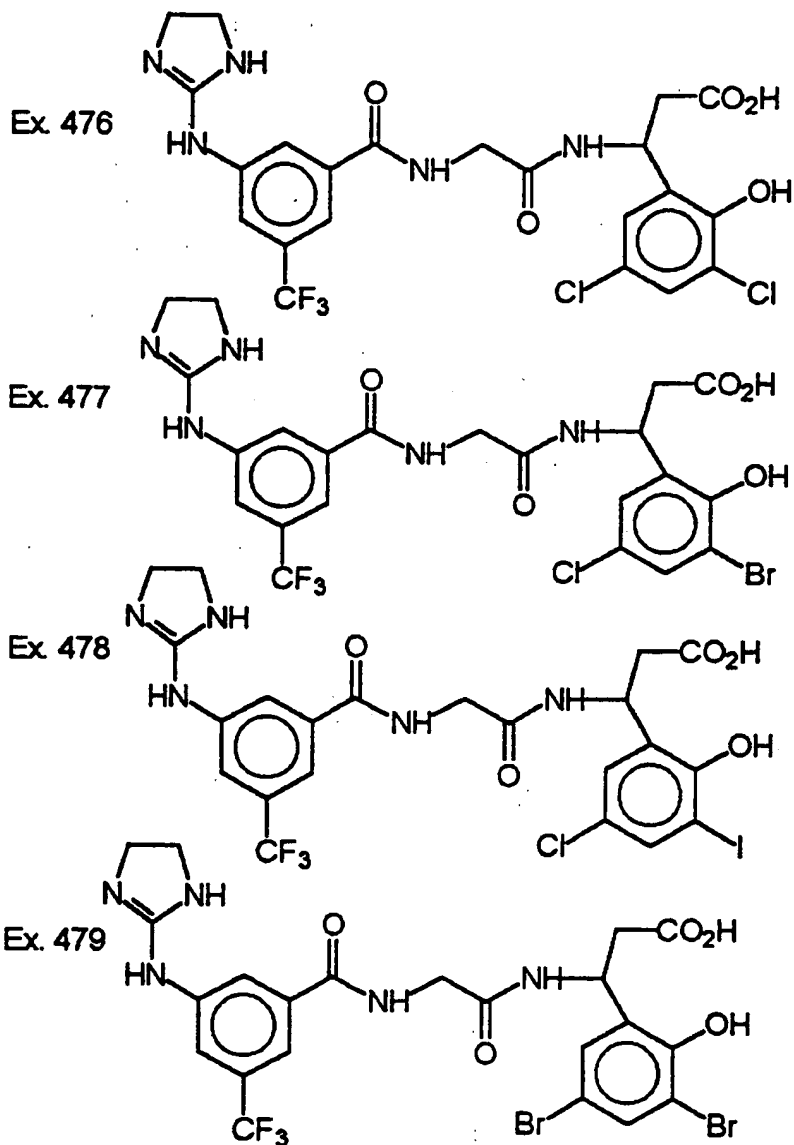
10

The above compound was prepared according to the methodology of Example 474, substituting an equivalent amount of phenylchloroformate (Aldrich) for ethylchloroformate in Example 474, Step A and by heating the reaction mixture at 70°C for 8 hours then room temperature for 2 days in Example 474, Step B.

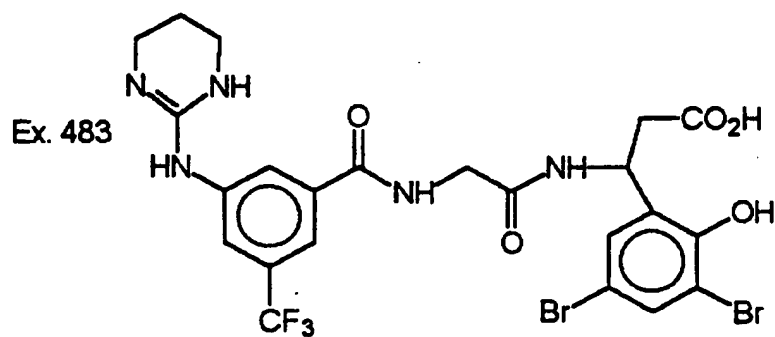
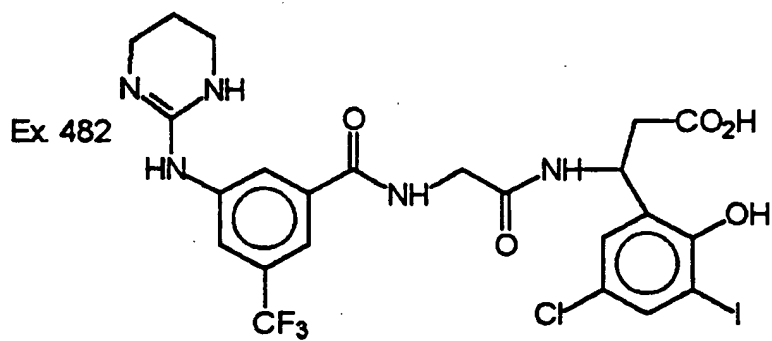
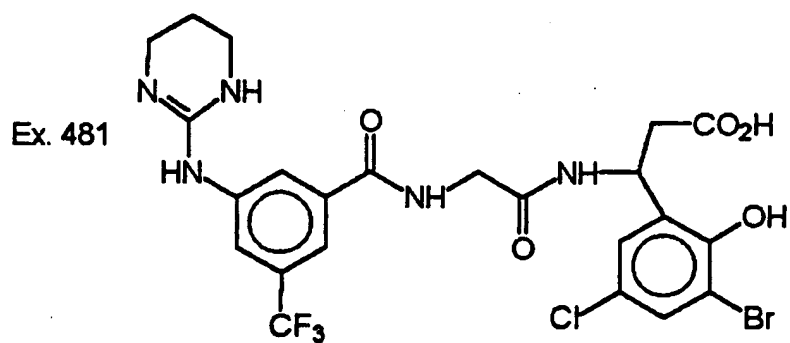
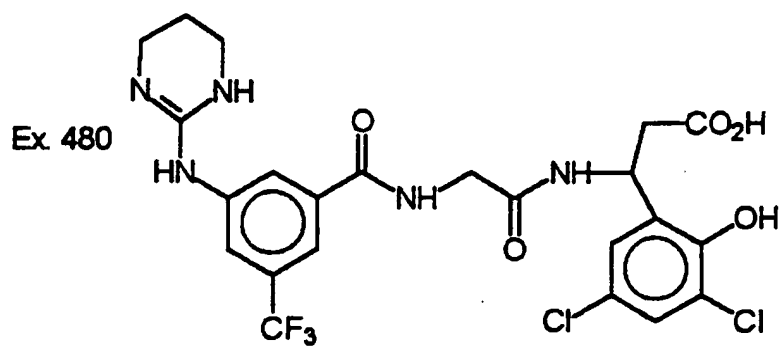
MS and NMR were consistent with the desired structure.

Using the methodologies, reagents and conditions exemplified in the schemes and examples of this disclosure (or the synthesis of reagents from readily available starting materials via methodologies known to those skilled in the art), the following compounds of the present invention are synthesized:

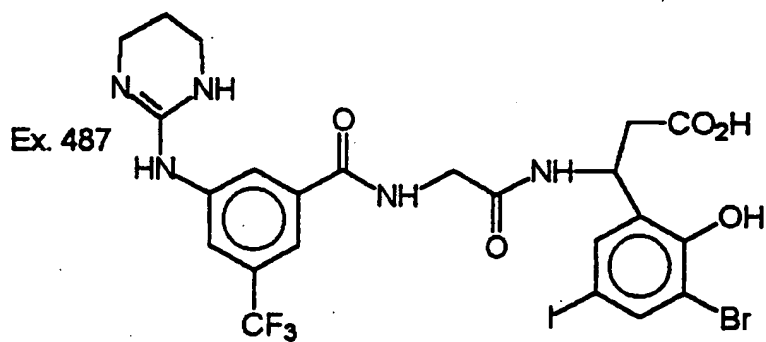
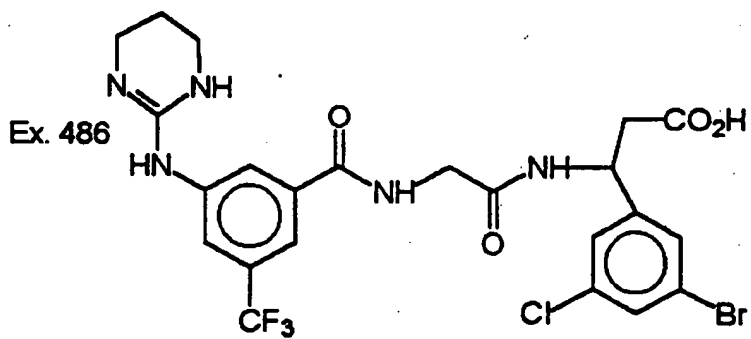
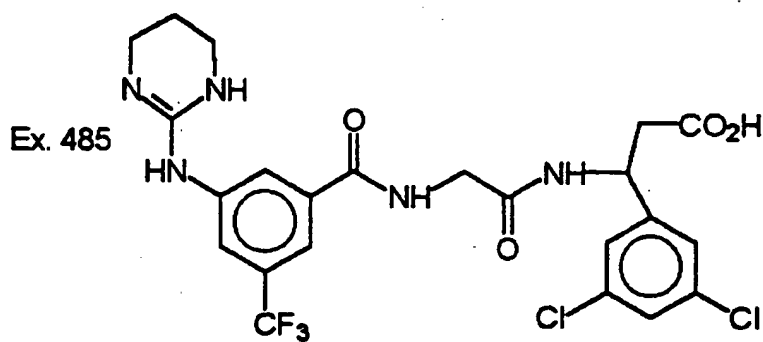
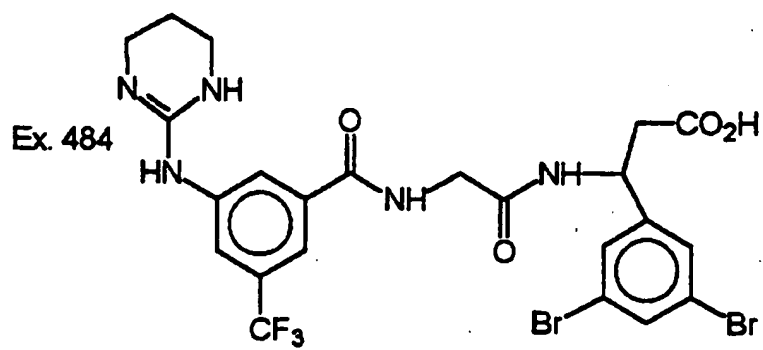
Examples 476-517



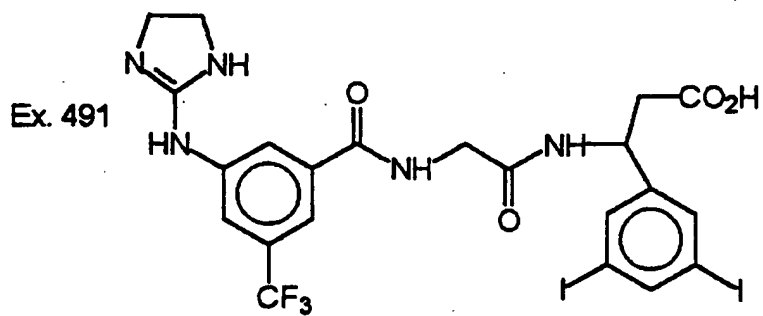
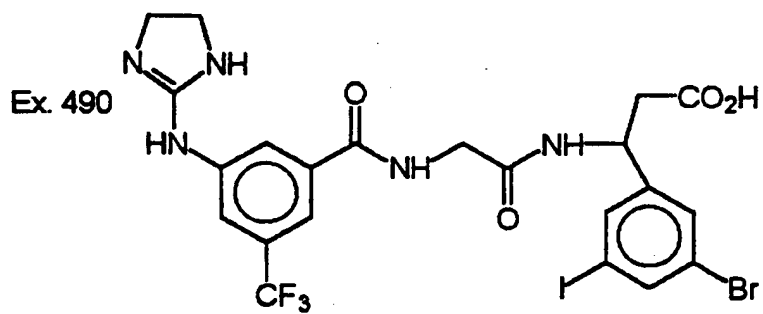
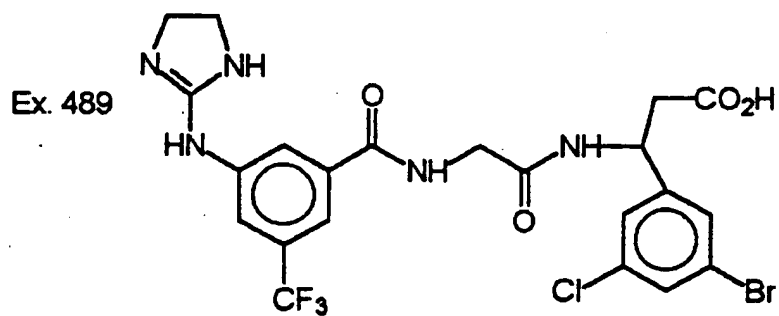
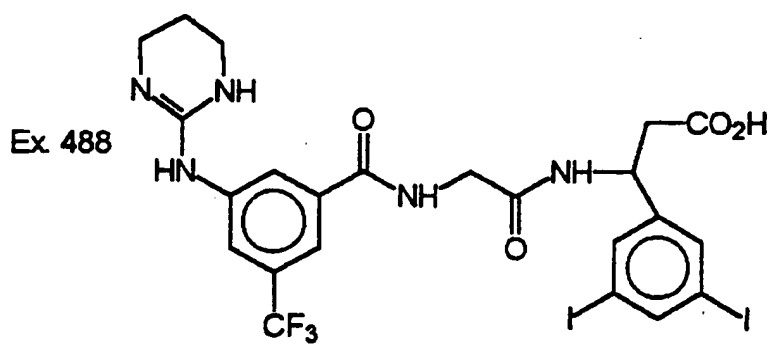
- 675 -

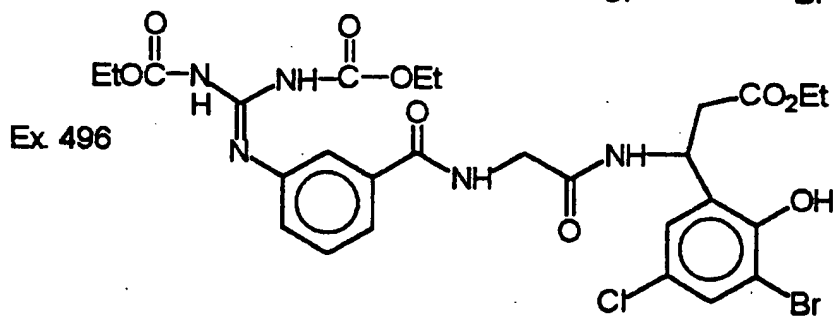
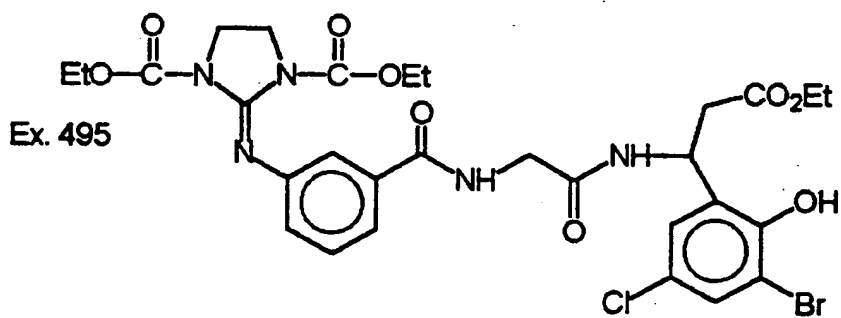
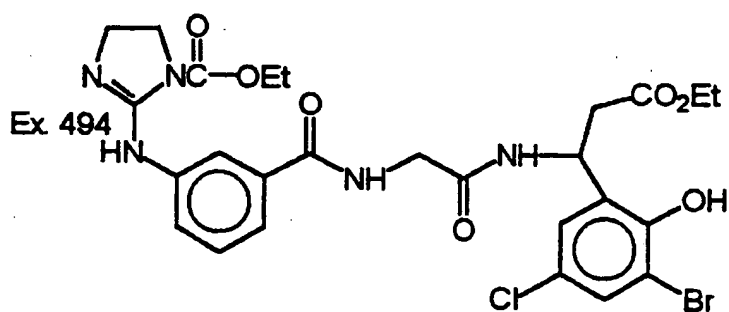
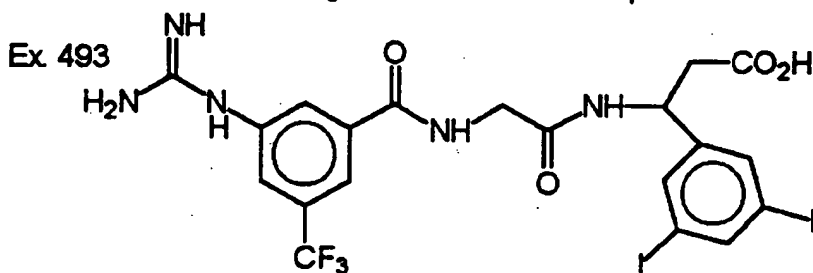
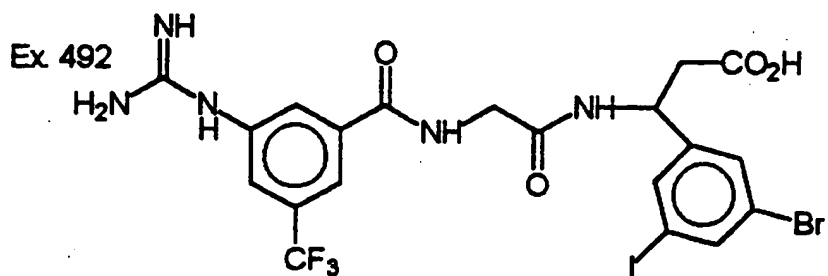


- 676 -

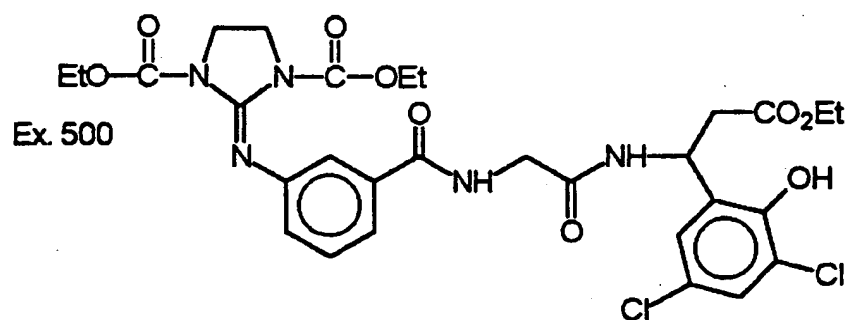
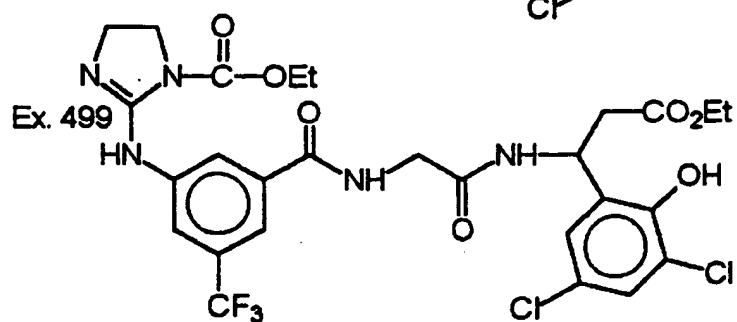
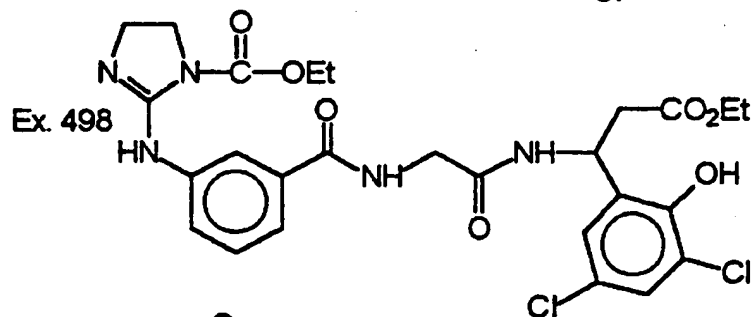
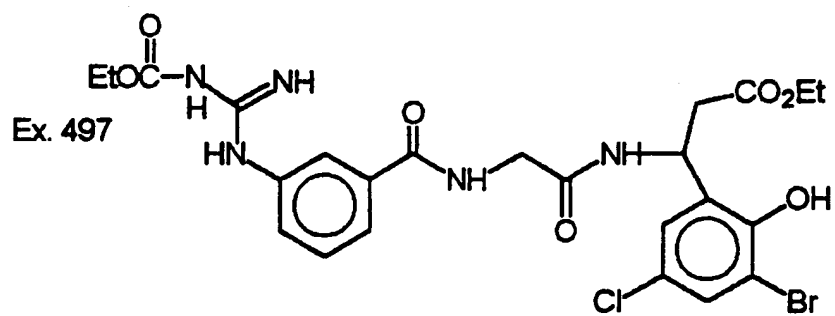


- 677 -

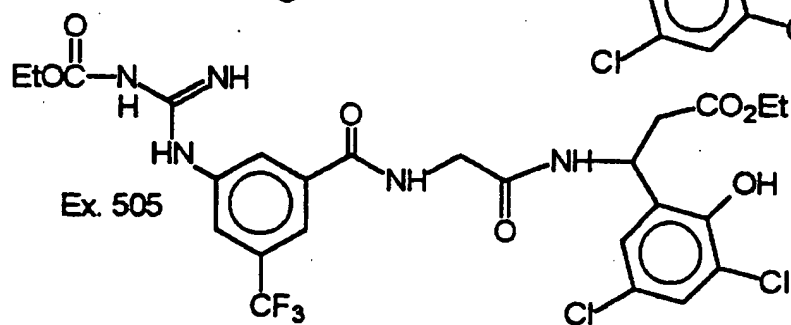
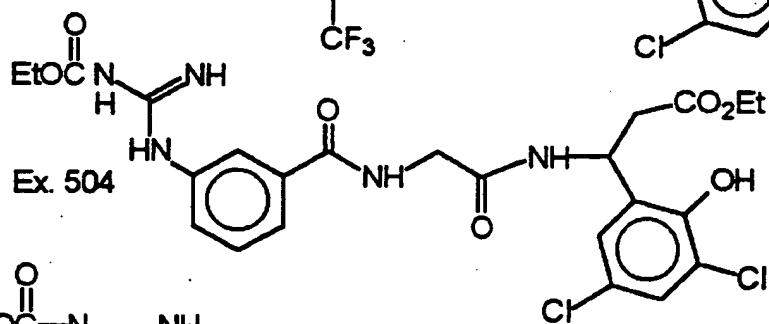
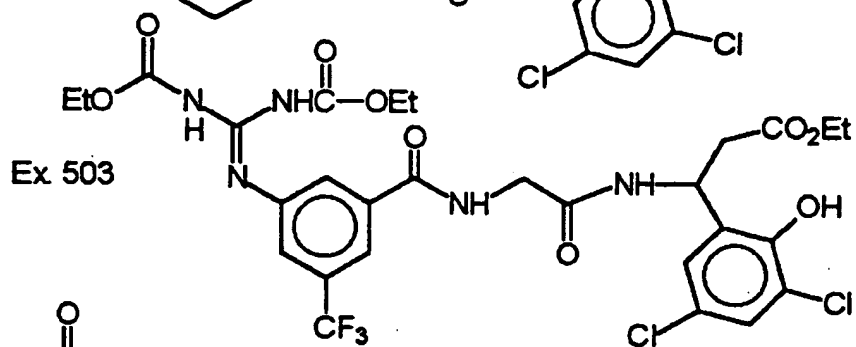
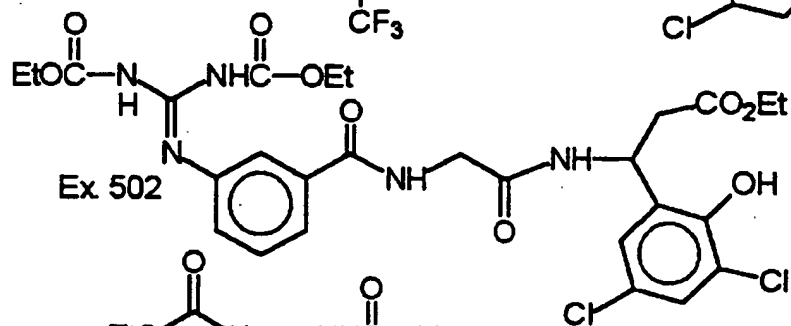
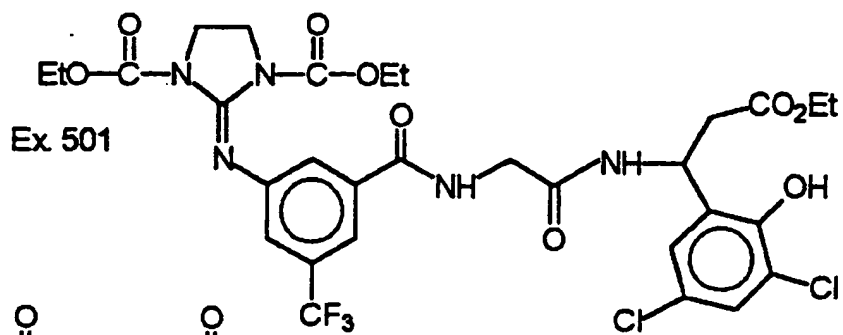




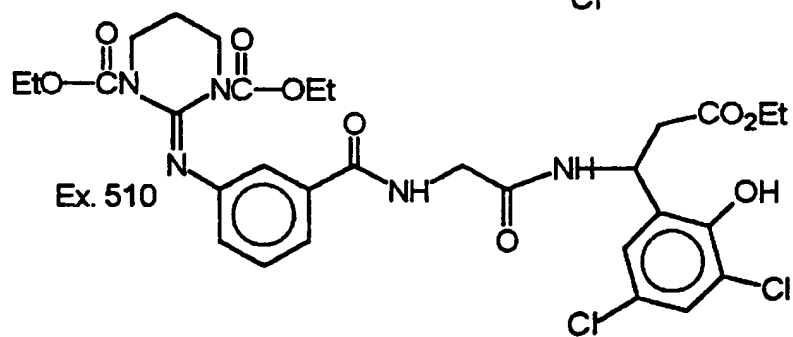
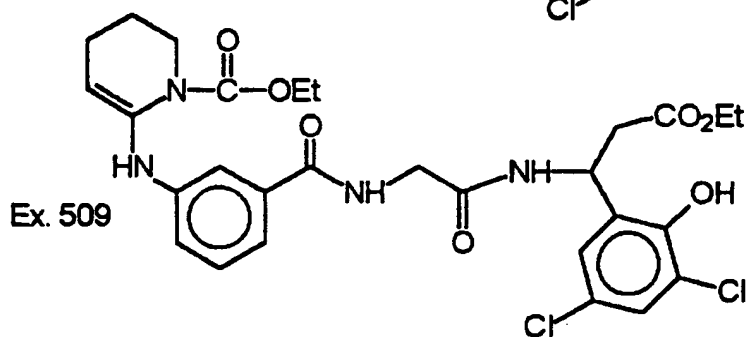
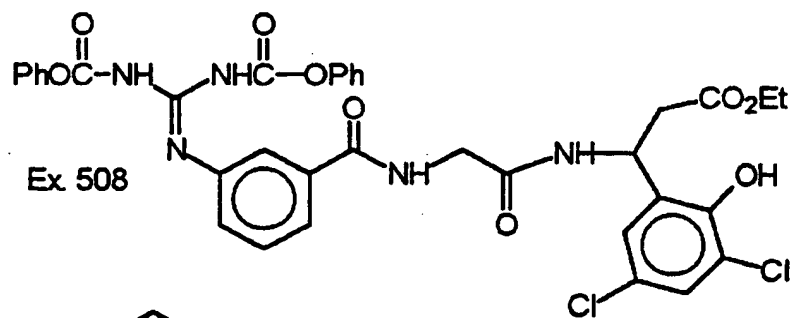
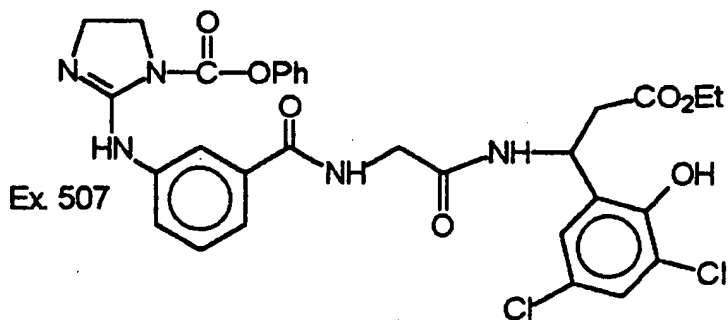
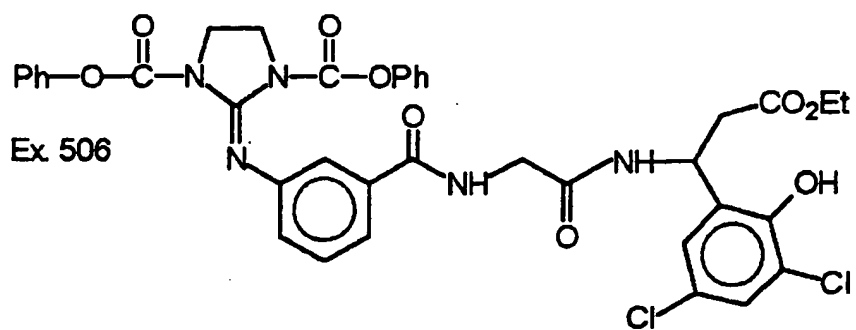
- 679 -

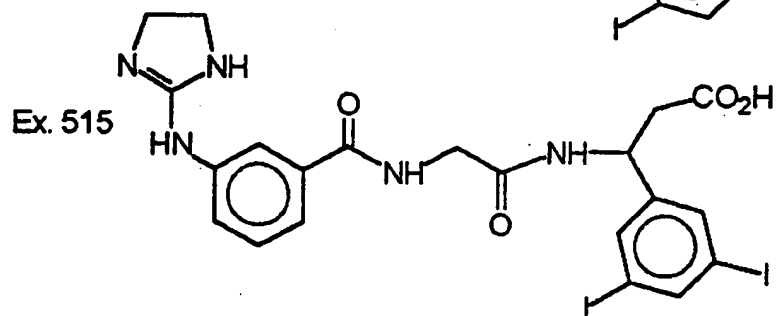
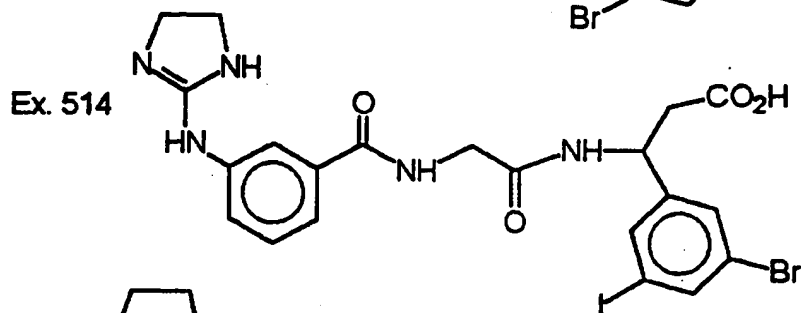
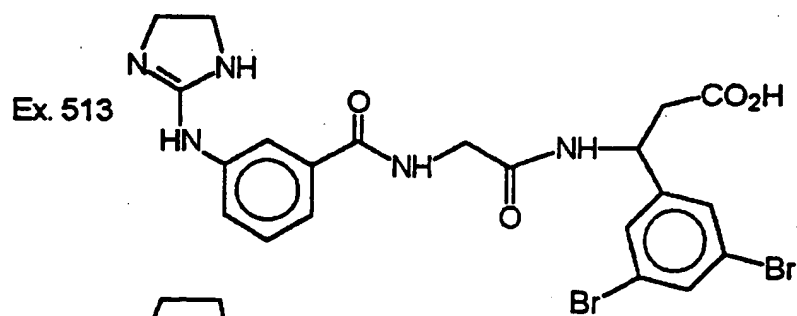
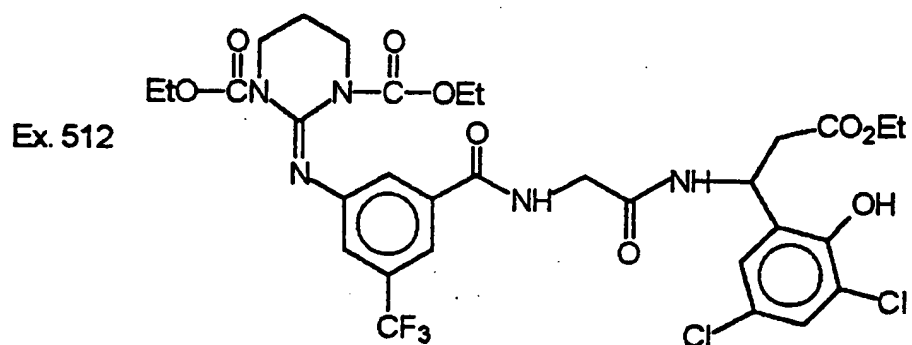
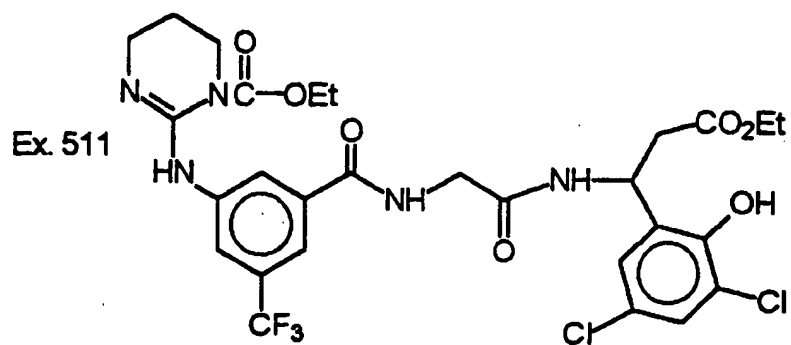


- 680 -

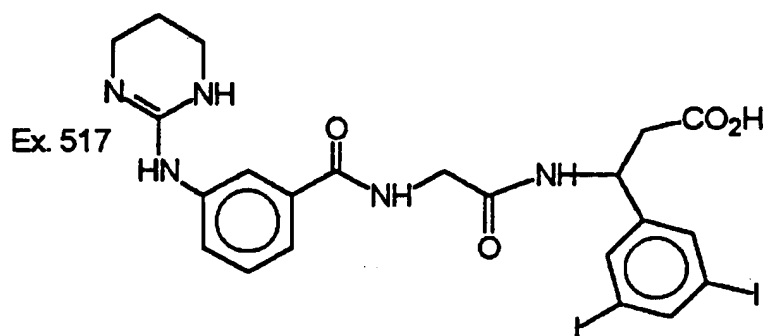
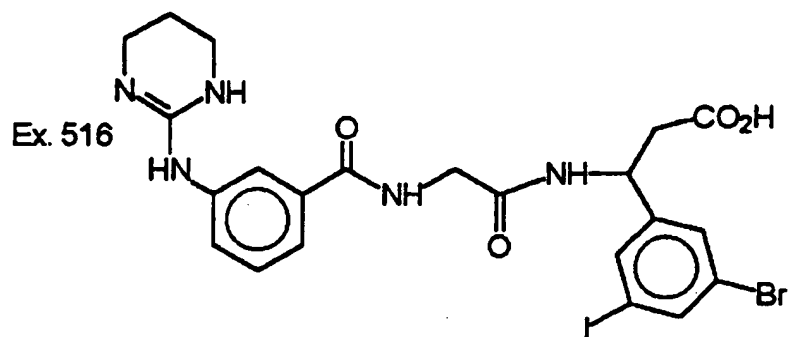


- 681 -



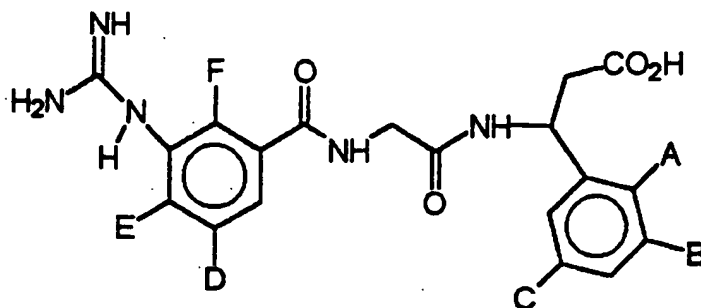


- 683 -



- 684 -

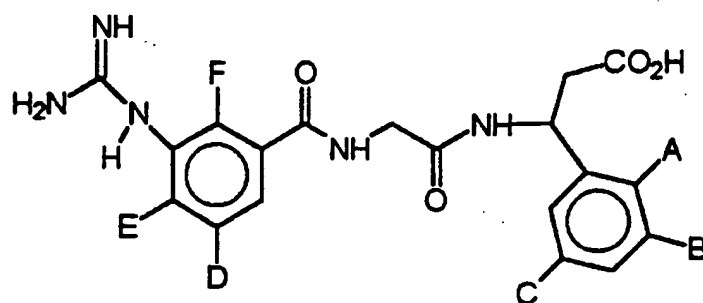
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 518 | OH | Cl | Cl | Br | H | H |
| | 519 | OH | Cl | Cl | OH | H | H |
| | 520 | OH | Cl | Cl | NO ₂ | H | H |
| | 521 | OH | Cl | Cl | I | H | H |
| | 522 | OH | Cl | Cl | Cl | H | H |
| 15 | 523 | OH | Cl | Cl | Cl | H | Cl |
| | 524 | OH | Cl | Cl | OMe | H | H |
| | 525 | OH | Cl | Cl | H | CF ₃ | H |
| | 526 | OH | Cl | Cl | H | OH | H |
| | 527 | OH | Cl | Cl | H | OMe | H |
| 20 | 528 | OH | Cl | Cl | H | Cl | H |
| | 529 | OH | Cl | Cl | H | Cl | Cl |
| | 530 | OH | Cl | Cl | H | Br | H |
| | 531 | OH | Cl | Cl | Cl | OH | H |
| | 532 | OH | Cl | Cl | Br | OH | H |
| 25 | 533 | OH | Cl | Cl | I | OH | H |

- 685 -

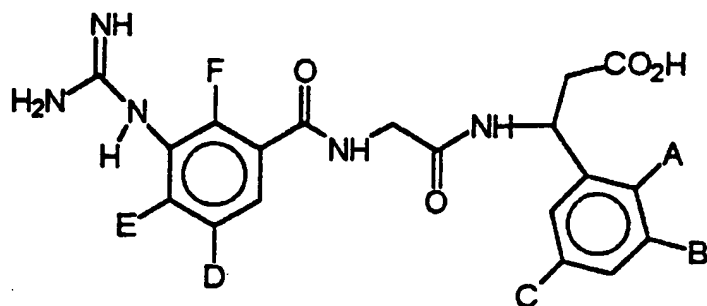
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 534 | OH | Br | Cl | Br | H | H |
| | 535 | OH | Br | Cl | OH | H | H |
| | 536 | OH | Br | Cl | NO ₂ | H | H |
| | 537 | OH | Br | Cl | I | H | H |
| | 538 | OH | Br | Cl | Cl | H | H |
| 15 | 539 | OH | Br | Cl | Cl | H | Cl |
| | 540 | OH | Br | Cl | OMe | H | H |
| | 541 | OH | Br | Cl | H | CF ₃ | H |
| | 542 | OH | Br | Cl | H | OH | H |
| | 543 | OH | Br | Cl | H | OMe | H |
| 20 | 544 | OH | Br | Cl | H | Cl | H |
| | 545 | OH | Br | Cl | H | Cl | Cl |
| | 546 | OH | Br | Cl | H | Br | H |
| | 547 | OH | Br | Cl | Cl | OH | H |
| | 548 | OH | Br | Cl | Br | OH | H |
| 25 | 549 | OH | Br | Cl | I | OH | H |

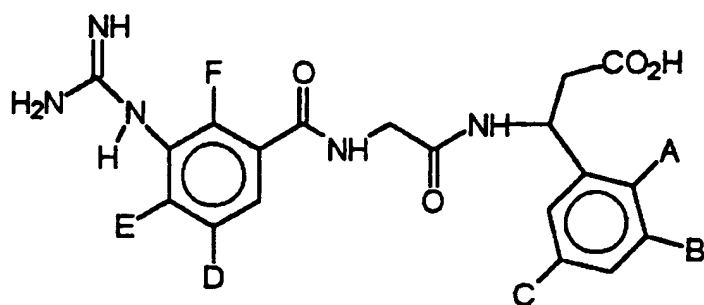
- 686 -

5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 550 | OH | I | Cl | Br | H | H |
| | 551 | OH | I | Cl | OH | H | H |
| | 552 | OH | I | Cl | NO ₂ | H | H |
| | 553 | OH | I | Cl | I | H | H |
| | 554 | OH | I | Cl | Cl | H | H |
| 15 | 555 | OH | I | Cl | Cl | H | Cl |
| | 556 | OH | I | Cl | OMe | H | H |
| | 557 | OH | I | Cl | H | CF ₃ | H |
| | 558 | OH | I | Cl | H | OH | H |
| | 559 | OH | I | Cl | H | OMe | H |
| 20 | 560 | OH | I | Cl | H | Cl | H |
| | 561 | OH | I | Cl | H | Cl | Cl |
| | 562 | OH | I | Cl | H | Br | H |
| | 563 | OH | I | Cl | CF ₃ | H | H |
| | 564 | OH | I | Cl | Cl | OH | H |
| 25 | 565 | OH | I | Cl | Br | OH | H |
| | 566 | OH | I | Cl | I | OH | H |

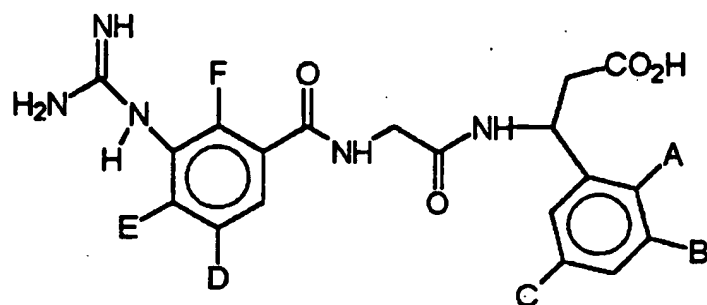
- 687 -



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 567 | H | Br | Cl | Br | H | H |
| | 568 | H | Br | Cl | OH | H | H |
| | 569 | H | Br | Cl | NO ₂ | H | H |
| | 570 | H | Br | Cl | I | H | H |
| | 571 | H | Br | Cl | Cl | H | H |
| 15 | 572 | H | Br | Cl | Cl | H | Cl |
| | 573 | H | Br | Cl | OMe | H | H |
| | 574 | H | Br | Cl | H | CF ₃ | H |
| | 575 | H | Br | Cl | H | OH | H |
| | 576 | H | Br | Cl | H | OMe | H |
| 20 | 577 | H | Br | Cl | H | Cl | H |
| | 578 | H | Br | Cl | H | Cl | Cl |
| | 579 | H | Br | Cl | H | Br | H |
| | 580 | H | Br | Cl | Cl | OH | H |
| | 581 | H | Br | Cl | Br | OH | H |
| 25 | 582 | H | Br | Cl | I | OH | H |

- 688 -

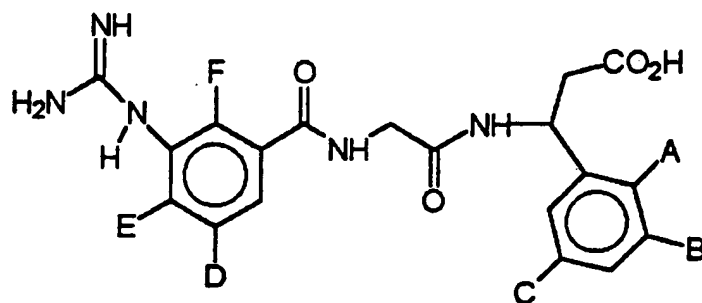
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 583 | H | Br | Br | Br | H | H |
| | 584 | H | Br | Br | OH | H | H |
| | 585 | H | Br | Br | NO ₂ | H | H |
| | 586 | H | Br | Br | I | H | H |
| | 587 | H | Br | Br | Cl | H | H |
| | 588 | H | Br | Br | Cl | H | Cl |
| | 589 | H | Br | Br | OMe | H | H |
| 15 | 590 | H | Br | Br | H | CF ₃ | H |
| | 591 | H | Br | Br | H | OH | H |
| | 592 | H | Br | Br | H | OMe | H |
| | 593 | H | Br | Br | H | Cl | H |
| | 594 | H | Br | Br | H | Cl | Cl |
| | 595 | H | Br | Br | H | Br | H |
| | 596 | H | Br | Br | Cl | OH | H |
| 20 | 597 | H | Br | Br | Br | OH | H |
| | 598 | H | Br | Br | I | OH | H |
| | 599 | H | Br | Br | I | OH | H |

- 689 -

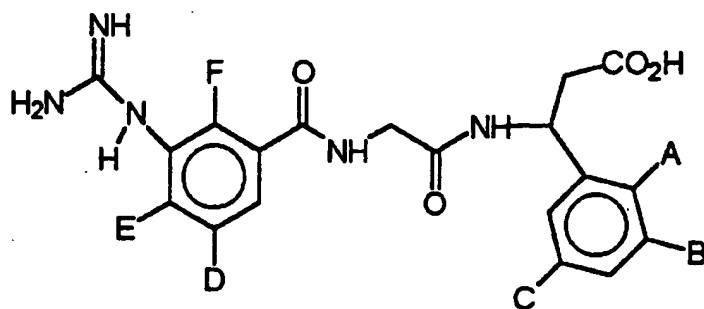
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 599 | H | Br | I | Br | H | H |
| | 600 | H | Br | I | OH | H | H |
| | 601 | H | Br | I | NO ₂ | H | H |
| | 602 | H | Br | I | I | H | H |
| | 603 | H | Br | I | Cl | H | H |
| 15 | 604 | H | Br | I | Cl | H | Cl |
| | 605 | H | Br | I | OMe | H | H |
| | 606 | H | Br | I | H | CF ₃ | H |
| | 607 | H | Br | I | H | OH | H |
| | 608 | H | Br | I | H | OMe | H |
| 20 | 609 | H | Br | I | H | Cl | H |
| | 610 | H | Br | I | H | Cl | Cl |
| | 611 | H | Br | I | H | Br | H |
| | 612 | H | Br | I | Cl | OH | H |
| | 613 | H | Br | I | Br | OH | H |
| 25 | 614 | H | Br | I | I | OH | H |

- 690 -

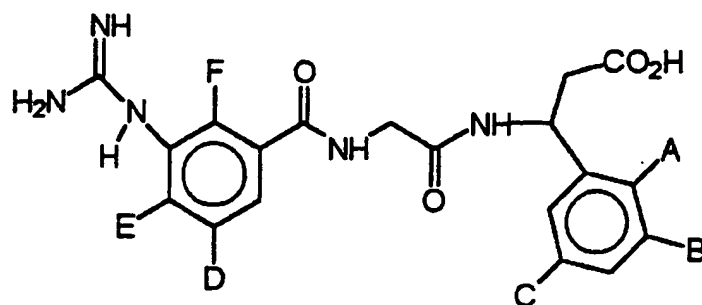
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 615 | H | I | I | Br | H | H |
| | 616 | H | I | I | OH | H | H |
| | 617 | H | I | I | NO ₂ | H | H |
| | 618 | H | I | I | I | H | H |
| | 619 | H | I | I | Cl | H | H |
| 15 | 620 | H | I | I | Cl | H | Cl |
| | 621 | H | I | I | OMe | H | H |
| | 622 | H | I | I | H | CF ₃ | H |
| | 623 | H | I | I | H | OH | H |
| | 624 | H | I | I | H | OMe | H |
| 20 | 625 | H | I | I | H | Cl | H |
| | 626 | H | I | I | H | Cl | Cl |
| | 627 | H | I | I | H | Br | H |
| | 628 | H | I | I | Cl | OH | H |
| | 629 | H | I | I | Br | OH | H |
| 25 | 630 | H | I | I | I | OH | H |

- 691 -

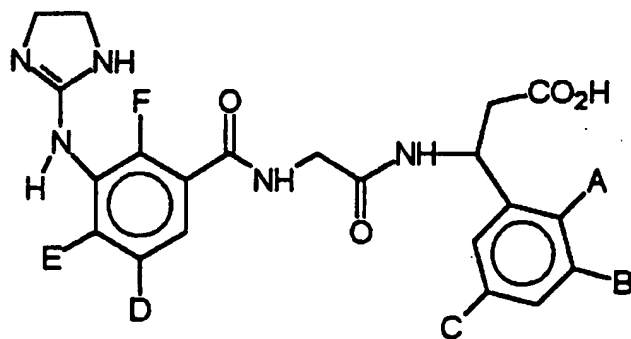
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 631 | H | Cl | Cl | Br | H | H |
| | 632 | H | Cl | Cl | OH | H | H |
| | 633 | H | Cl | Cl | NO ₂ | H | H |
| | 634 | H | Cl | Cl | I | H | H |
| | 635 | H | Cl | Cl | Cl | H | H |
| 15 | 636 | H | Cl | Cl | Cl | H | Cl |
| | 637 | H | Cl | Cl | OMe | H | H |
| | 638 | H | Cl | Cl | H | CF ₃ | H |
| | 639 | H | Cl | Cl | H | OH | H |
| | 640 | H | Cl | Cl | H | OMe | H |
| 20 | 641 | H | Cl | Cl | H | Cl | H |
| | 642 | H | Cl | Cl | H | Cl | Cl |
| | 643 | H | Cl | Cl | H | Br | H |
| | 644 | H | Cl | Cl | Cl | OH | H |
| | 645 | H | Cl | Cl | Br | OH | H |
| 25 | 646 | H | Cl | Cl | I | OH | H |

- 692 -

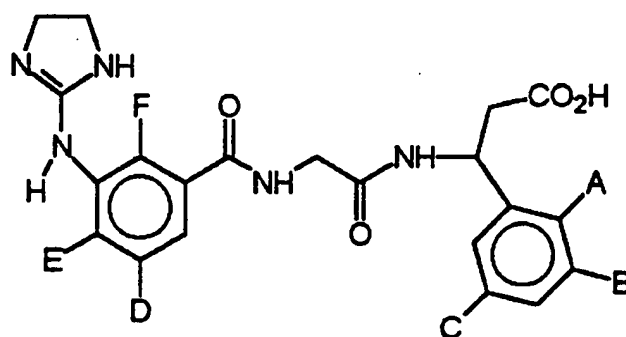
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 647 | OH | Cl | Cl | Br | H | H |
| | 648 | OH | Cl | Cl | OH | H | H |
| | 649 | OH | Cl | Cl | NO ₂ | H | H |
| | 650 | OH | Cl | Cl | I | H | H |
| | 651 | OH | Cl | Cl | Cl | H | H |
| | 652 | OH | Cl | Cl | Cl | H | Cl |
| 15 | 653 | OH | Cl | Cl | OMe | H | H |
| | 654 | OH | Cl | Cl | H | CF ₃ | H |
| | 655 | OH | Cl | Cl | H | OH | H |
| | 656 | OH | Cl | Cl | H | OMe | H |
| | 657 | OH | Cl | Cl | H | Cl | H |
| 20 | 658 | OH | Cl | Cl | H | Cl | Cl |
| | 659 | OH | Cl | Cl | H | Br | H |
| | 660 | OH | Cl | Cl | Cl | OH | H |
| | 661 | OH | Cl | Cl | Br | OH | H |
| | 662 | OH | Cl | Cl | I | OH | H |

- 693 -

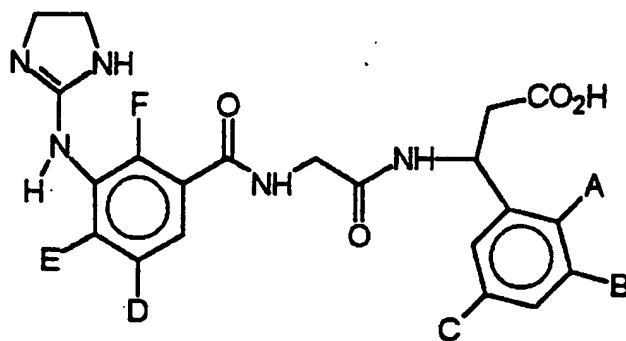
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 663 | OH | Br | Cl | Br | H | H |
| | 664 | OH | Br | Cl | OH | H | H |
| | 665 | OH | Br | Cl | NO ₂ | H | H |
| | 666 | OH | Br | Cl | I | H | H |
| | 667 | OH | Br | Cl | Cl | H | H |
| 15 | 668 | OH | Br | Cl | Cl | H | Cl |
| | 669 | OH | Br | Cl | OMe | H | H |
| | 670 | OH | Br | Cl | H | CF ₃ | H |
| | 671 | OH | Br | Cl | H | OH | H |
| | 672 | OH | Br | Cl | H | OMe | H |
| 20 | 673 | OH | Br | Cl | H | Cl | H |
| | 674 | OH | Br | Cl | H | Cl | Cl |
| | 675 | OH | Br | Cl | H | Br | H |
| | 676 | OH | Br | Cl | Cl | OH | H |
| | 677 | OH | Br | Cl | Br | OH | H |
| 25 | 678 | OH | Br | Cl | I | OH | H |

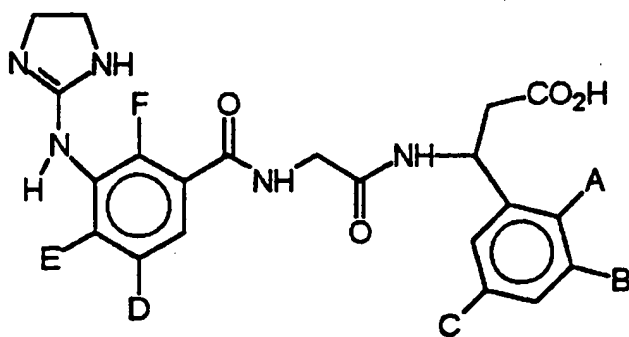
- 694 -

5

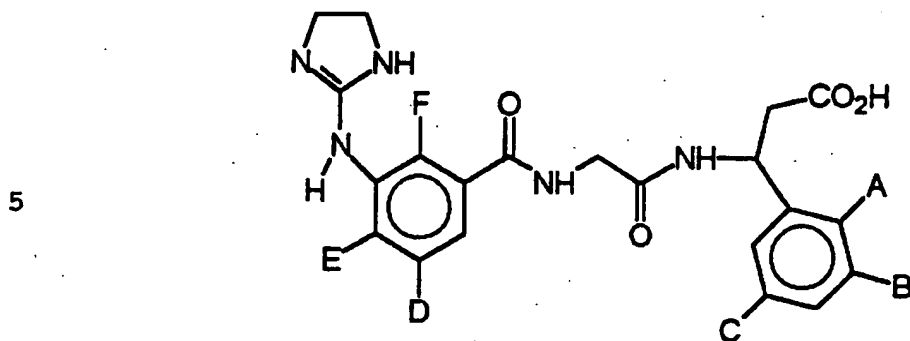


| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 679 | OH | I | Cl | Br | H | H |
| | 680 | OH | I | Cl | OH | H | H |
| | 681 | OH | I | Cl | NO ₂ | H | H |
| | 682 | OH | I | Cl | I | H | H |
| | 683 | OH | I | Cl | Cl | H | H |
| 15 | 684 | OH | I | Cl | Cl | H | Cl |
| | 685 | OH | I | Cl | OMe | H | H |
| | 686 | OH | I | Cl | H | CF ₃ | H |
| | 687 | OH | I | Cl | H | OH | H |
| | 688 | OH | I | Cl | H | OMe | H |
| 20 | 689 | OH | I | Cl | H | Cl | H |
| | 690 | OH | I | Cl | H | Cl | Cl |
| | 691 | OH | I | Cl | H | Br | H |
| | 692 | OH | I | Cl | Cl | OH | H |
| | 693 | OH | I | Cl | Br | OH | H |
| 25 | 694 | OH | I | Cl | I | OH | H |

- 695 -



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 695 | H | Cl | Cl | Br | H | H |
| | 696 | H | Cl | Cl | OH | H | H |
| | 697 | H | Cl | Cl | NO ₂ | H | H |
| | 698 | H | Cl | Cl | I | H | H |
| | 699 | H | Cl | Cl | Cl | H | H |
| 15 | 700 | H | Cl | Cl | Cl | H | Cl |
| | 701 | H | Cl | Cl | OMe | H | H |
| | 702 | H | Cl | Cl | H | CF ₃ | H |
| | 703 | H | Cl | Cl | H | OH | H |
| | 704 | H | Cl | Cl | H | OMe | H |
| 20 | 705 | H | Cl | Cl | H | Cl | H |
| | 706 | H | Cl | Cl | H | Cl | Cl |
| | 707 | H | Cl | Cl | H | Br | H |
| | 708 | H | Cl | Cl | Cl | OH | H |
| | 709 | H | Cl | Cl | Br | OH | H |
| 25 | 710 | H | Cl | Cl | I | OH | H |

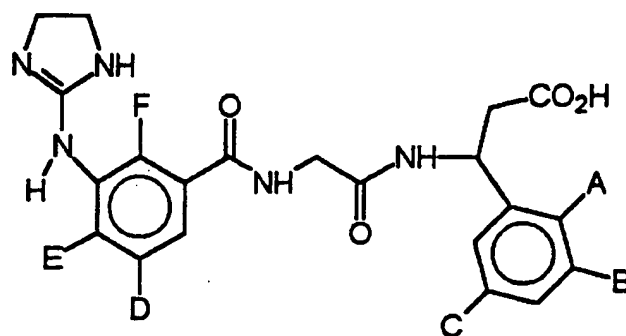


| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 711 | H | Br | Cl | Br | H | H |
| | 712 | H | Br | Cl | OH | H | H |
| | 713 | H | Br | Cl | NO ₂ | H | H |
| | 714 | H | Br | Cl | I | H | H |
| | 715 | H | Br | Cl | Cl | H | H |
| 15 | 716 | H | Br | Cl | Cl | H | Cl |
| | 717 | H | Br | Cl | OMe | H | H |
| | 718 | H | Br | Cl | H | CF ₃ | H |
| | 719 | H | Br | Cl | H | OH | H |
| | 720 | H | Br | Cl | H | OMe | H |
| 20 | 721 | H | Br | Cl | H | Cl | H |
| | 722 | H | Br | Cl | H | Cl | Cl |
| | 723 | H | Br | Cl | H | Br | H |
| | 724 | H | Br | Cl | Cl | OH | H |
| | 725 | H | Br | Cl | Br | OH | H |
| | 726 | H | Br | Cl | I | OH | H |

25

- 697 -

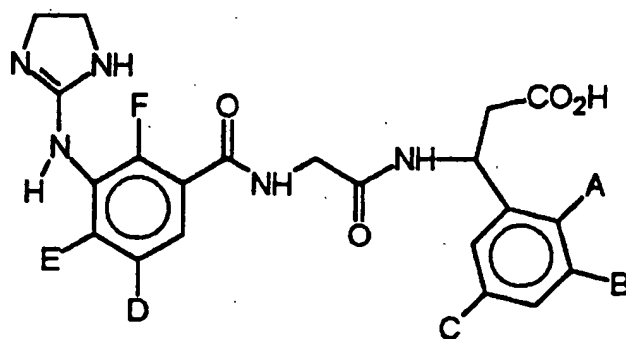
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 727 | H | Br | Br | Br | H | H |
| | 728 | H | Br | Br | OH | H | H |
| | 729 | H | Br | Br | NO ₂ | H | H |
| | 730 | H | Br | Br | I | H | H |
| | 731 | H | Br | Br | Cl | H | H |
| 15 | 732 | H | Br | Br | Cl | H | Cl |
| | 733 | H | Br | Br | OMe | H | H |
| | 734 | H | Br | Br | H | CF ₃ | H |
| | 735 | H | Br | Br | H | OH | H |
| | 736 | H | Br | Br | H | OMe | H |
| 20 | 737 | H | Br | Br | H | Cl | H |
| | 738 | H | Br | Br | H | Cl | Cl |
| | 739 | H | Br | Br | H | Br | H |
| | 740 | H | Br | Br | Cl | OH | H |
| | 741 | H | Br | Br | Br | OH | H |
| 25 | 742 | H | Br | Br | I | OH | H |

- 698 -

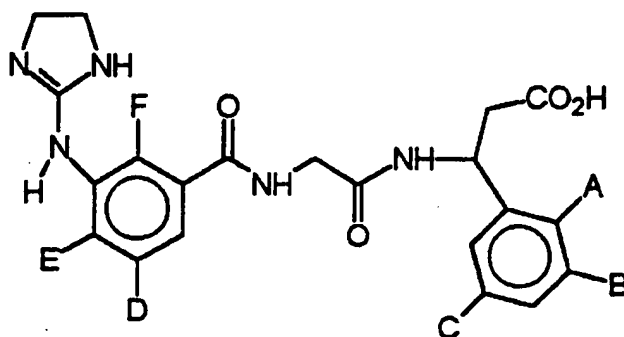
5



| <u>Example #</u> | | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|------------------|-----|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 743 | H | Br | I | Br | H | H |
| | 744 | H | Br | I | OH | H | H |
| | 745 | H | Br | I | NO ₂ | H | H |
| | 746 | H | Br | I | I | H | H |
| | 747 | H | Br | I | Cl | H | H |
| 15 | 748 | H | Br | I | Cl | H | Cl |
| | 749 | H | Br | I | OMe | H | H |
| | 750 | H | Br | I | H | CF ₃ | H |
| | 751 | H | Br | I | H | OH | H |
| | 752 | H | Br | I | H | OMe | H |
| 20 | 753 | H | Br | I | H | Cl | H |
| | 754 | H | Br | I | H | Cl | Cl |
| | 755 | H | Br | I | H | Br | H |
| | 756 | H | Br | I | Cl | OH | H |
| | 757 | H | Br | I | Br | OH | H |
| 25 | 758 | H | Br | I | I | OH | H |

- 699 -

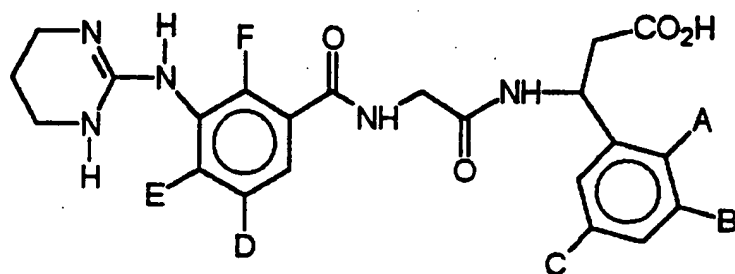
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 759 | H | I | I | Br | H | H |
| | 760 | H | I | I | OH | H | H |
| | 761 | H | I | I | NO ₂ | H | H |
| | 762 | H | I | I | I | H | H |
| | 763 | H | I | I | Cl | H | H |
| 15 | 764 | H | I | I | Cl | H | Cl |
| | 765 | H | I | I | OMe | H | H |
| | 766 | H | I | I | H | CF ₃ | H |
| | 767 | H | I | I | H | OH | H |
| | 768 | H | I | I | H | OMe | H |
| 20 | 769 | H | I | I | H | Cl | H |
| | 770 | H | I | I | H | Cl | Cl |
| | 771 | H | I | I | H | Br | H |
| | 772 | H | I | I | Cl | OH | H |
| | 773 | H | I | I | Br | OH | H |
| 25 | 774 | H | I | I | I | OH | H |

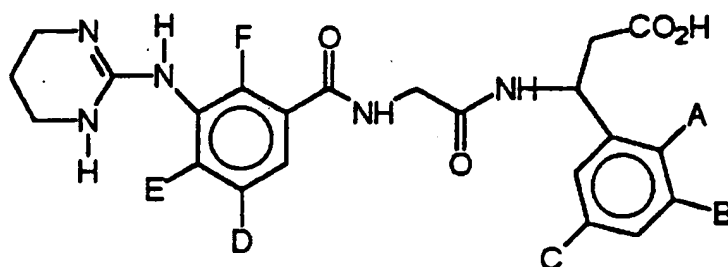
- 700 -

5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 775 | OH | Cl | Cl | Br | H | H |
| | 776 | OH | Cl | Cl | OH | H | H |
| | 777 | OH | Cl | Cl | NO ₂ | H | H |
| | 778 | OH | Cl | Cl | I | H | H |
| | 779 | OH | Cl | Cl | Cl | H | H |
| 15 | 780 | OH | Cl | Cl | Cl | H | Cl |
| | 781 | OH | Cl | Cl | OMe | H | H |
| | 782 | OH | Cl | Cl | H | CF ₃ | H |
| | 783 | OH | Cl | Cl | H | OH | H |
| | 784 | OH | Cl | Cl | H | OMe | H |
| 20 | 785 | OH | Cl | Cl | H | Cl | H |
| | 786 | OH | Cl | Cl | H | Cl | Cl |
| | 787 | OH | Cl | Cl | H | Br | H |
| | 788 | OH | Cl | Cl | Cl | OH | H |
| | 789 | OH | Cl | Cl | Br | OH | H |
| 25 | 790 | OH | Cl | Cl | I | OH | H |

- 701 -



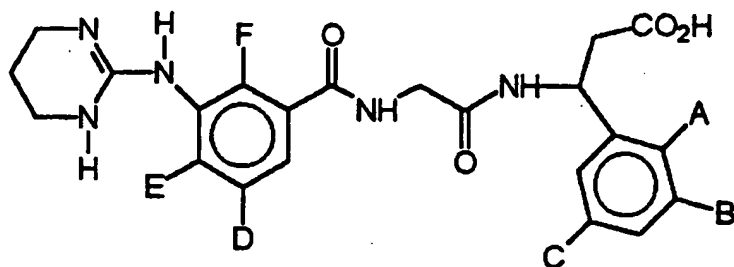
5

| <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 791 | OH | Br | Cl | Br | H | H |
| 10 792 | OH | Br | Cl | OH | H | H |
| 793 | OH | Br | Cl | NO ₂ | H | H |
| 794 | OH | Br | Cl | I | H | H |
| 795 | OH | Br | Cl | Cl | H | H |
| 796 | OH | Br | Cl | Cl | H | Cl |
| 15 797 | OH | Br | Cl | OMe | H | H |
| 798 | OH | Br | Cl | H | CF ₃ | H |
| 799 | OH | Br | Cl | H | OH | H |
| 800 | OH | Br | Cl | H | OMe | H |
| 801 | OH | Br | Cl | H | Cl | H |
| 20 802 | OH | Br | Cl | H | Cl | Cl |
| 803 | OH | Br | Cl | H | Br | H |
| 804 | OH | Br | Cl | Cl | OH | H |
| 805 | OH | Br | Cl | Br | OH | H |
| 806 | OH | Br | Cl | I | OH | H |

25

- 702 -

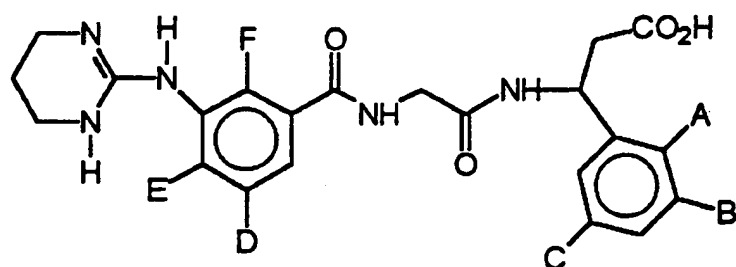
5



| <u>Example #</u> | | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|------------------|-----|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 807 | OH | I | Cl | Br | H | H |
| | 808 | OH | I | Cl | OH | H | H |
| | 809 | OH | I | Cl | NO ₂ | H | H |
| | 810 | OH | I | Cl | I | H | H |
| | 811 | OH | I | Cl | Cl | H | H |
| 15 | 812 | OH | I | Cl | Cl | H | Cl |
| | 813 | OH | I | Cl | OMe | H | H |
| | 814 | OH | I | Cl | H | CF ₃ | H |
| | 815 | OH | I | Cl | H | OH | H |
| | 816 | OH | I | Cl | H | OMe | H |
| 20 | 817 | OH | I | Cl | H | Cl | H |
| | 818 | OH | I | Cl | H | Cl | Cl |
| | 819 | OH | I | Cl | H | Br | H |
| | 820 | OH | I | Cl | Cl | OH | H |
| | 821 | OH | I | Cl | Br | OH | H |
| 25 | 822 | OH | I | Cl | I | OH | H |

- 703 -

5

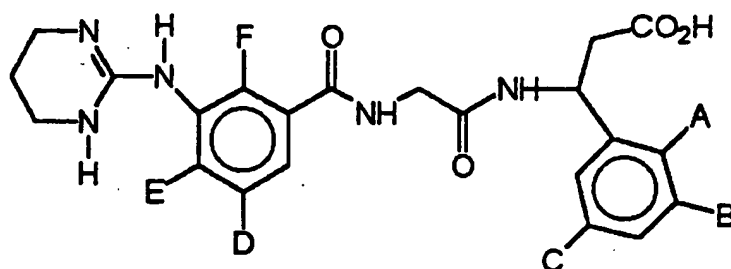


| <u>Example #</u> | | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|------------------|-----|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 823 | H | Cl | Cl | Br | H | H |
| | 824 | H | Cl | Cl | H | H | H |
| | 825 | H | Cl | Cl | NO ₂ | H | H |
| | 826 | H | Cl | Cl | I | H | H |
| | 827 | H | Cl | Cl | Cl | H | H |
| | 828 | H | Cl | Cl | Cl | H | Cl |
| 15 | 829 | H | Cl | Cl | OMe | H | H |
| | 830 | H | Cl | Cl | H | CF ₃ | H |
| | 831 | H | Cl | Cl | H | OH | H |
| | 832 | H | Cl | Cl | H | OMe | H |
| | 833 | H | Cl | Cl | H | Cl | H |
| | 834 | H | Cl | Cl | H | Cl | Cl |
| 20 | 835 | H | Cl | Cl | H | Br | H |
| | 836 | H | Cl | Cl | Cl | OH | H |
| | 837 | H | Cl | Cl | Br | OH | H |
| | 838 | H | Cl | Cl | I | OH | H |

25

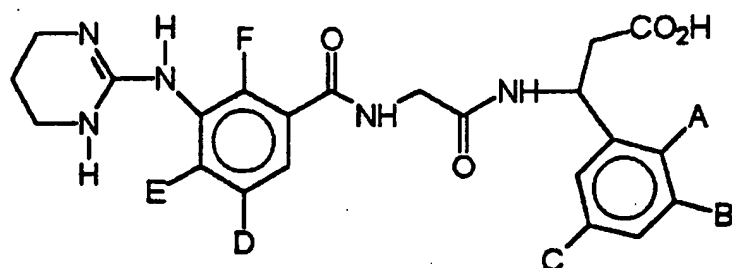
- 704 -

5



| <u>Example #</u> | | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|------------------|-----|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 839 | H | Br | Cl | Br | H | H |
| | 840 | H | Br | Cl | OH | H | H |
| | 841 | H | Br | Cl | NO ₂ | H | H |
| | 842 | H | Br | Cl | I | H | H |
| | 843 | H | Br | Cl | Cl | H | H |
| 15 | 845 | H | Br | Cl | Cl | H | Cl |
| | 846 | H | Br | Cl | OMe | H | H |
| | 847 | H | Br | Cl | H | CF ₃ | H |
| | 848 | H | Br | Cl | H | OH | H |
| | 849 | H | Br | Cl | H | OMe | H |
| 20 | 850 | H | Br | Cl | H | Cl | H |
| | 851 | H | Br | Cl | H | Cl | Cl |
| | 852 | H | Br | Cl | H | Br | H |
| | 853 | H | Br | Cl | Cl | OH | H |
| | 854 | H | Br | Cl | Br | OH | H |
| | 855 | H | Br | Cl | I | OH | H |
| 25 | | | | | | | |

- 705 -



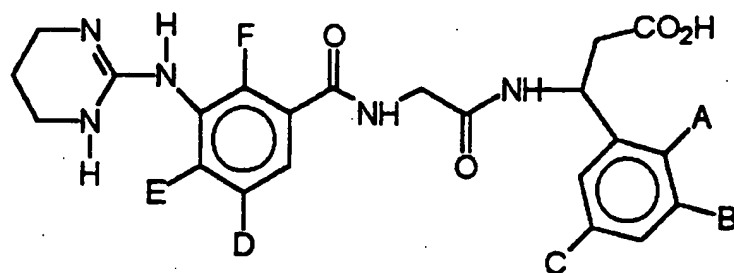
5

| <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 856 | H | Br | Br | Br | H | H |
| 10 857 | H | Br | Br | OH | H | H |
| 858 | H | Br | Br | NO ₂ | H | H |
| 859 | H | Br | Br | I | H | H |
| 860 | H | Br | Br | Cl | H | H |
| 861 | H | Br | Br | Cl | H | Cl |
| 15 862 | H | Br | Br | OMe | H | H |
| 863 | H | Br | Br | H | CF ₃ | H |
| 864 | H | Br | Br | H | OH | H |
| 865 | H | Br | Br | H | OMe | H |
| 866 | H | Br | Br | H | Cl | H |
| 20 867 | H | Br | Br | H | Cl | Cl |
| 868 | H | Br | Br | H | Br | H |
| 869 | H | Br | Br | Cl | OH | H |
| 870 | H | Br | Br | Br | OH | H |
| 871 | H | Br | Br | I | OH | H |

25

- 706 -

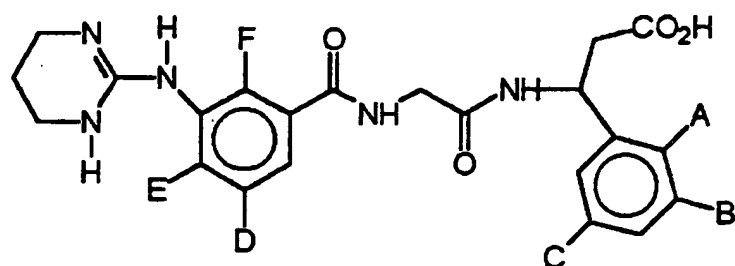
5



| <u>Example #</u> | | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|------------------|-----|----------|----------|----------|-----------------|-----------------|----------|
| 10 | 872 | H | Br | I | Br | H | H |
| | 873 | H | Br | I | OH | H | H |
| | 874 | H | Br | I | NO ₂ | H | H |
| | 875 | H | Br | I | I | H | H |
| | 876 | H | Br | I | Cl | H | H |
| 15 | 877 | H | Br | I | Cl | H | Cl |
| | 878 | H | Br | I | OMe | H | H |
| | 879 | H | Br | I | H | CF ₃ | H |
| | 880 | H | Br | I | H | OH | H |
| | 881 | H | Br | I | H | OMe | H |
| 20 | 882 | H | Br | I | H | Cl | H |
| | 883 | H | Br | I | H | Cl | Cl |
| | 884 | H | Br | I | H | Br | H |
| | 885 | H | Br | I | Cl | OH | H |
| | 886 | H | Br | I | Br | OH | H |
| | 887 | H | Br | I | I | OH | H |

25

- 707 -



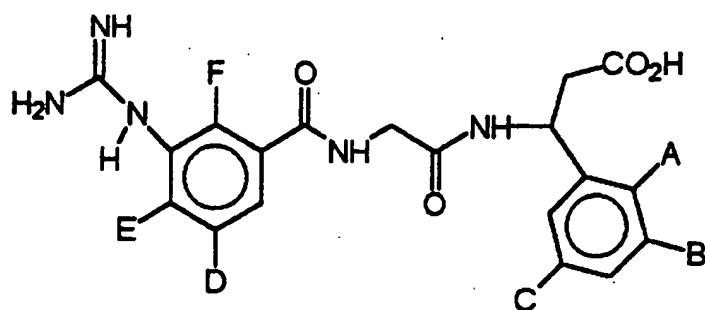
5

| <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|------------------|----------|----------|----------|-----------------|-----------------|----------|
| 888 | H | I | I | Br | H | H |
| 10 889 | H | I | I | OH | H | H |
| 890 | H | I | I | NO ₂ | H | H |
| 891 | H | I | I | I | H | H |
| 892 | H | I | I | Cl | H | H |
| 893 | H | I | I | Cl | H | Cl |
| 15 894 | H | I | I | OMe | H | H |
| 895 | H | I | I | H | CF ₃ | H |
| 896 | H | I | I | H | OH | H |
| 897 | H | I | I | H | OMe | H |
| 898 | H | I | I | H | Cl | H |
| 20 899 | H | I | I | H | Cl | Cl |
| 900 | H | I | I | H | Br | H |
| 901 | H | I | I | Cl | OH | H |
| 902 | H | I | I | Br | OH | H |
| 903 | H | I | I | I | OH | H |

25

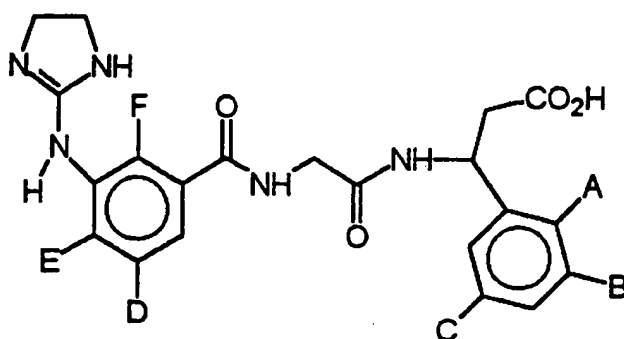
- 708 -

5



| <u>Example #</u> | | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|------------------|-----|----------|-----------------|----------|-----------------|-----------------|----------|
| 10 | 904 | H | CF ₃ | Br | Br | H | H |
| | 905 | H | CF ₃ | Br | OH | H | H |
| | 906 | H | CF ₃ | Br | NO ₂ | H | H |
| | 907 | H | CF ₃ | Br | I | H | H |
| | 908 | H | CF ₃ | Br | Cl | H | H |
| 15 | 909 | H | CF ₃ | Br | Cl | H | Cl |
| | 910 | H | CF ₃ | Br | OMe | H | H |
| | 911 | H | CF ₃ | Br | H | CF ₃ | H |
| | 912 | H | CF ₃ | Br | H | OH | H |
| | 913 | H | CF ₃ | Br | H | OMe | H |
| 20 | 914 | H | CF ₃ | Br | H | Cl | H |
| | 915 | H | CF ₃ | Br | H | Cl | Cl |
| | 916 | H | CF ₃ | Br | H | Br | H |
| | 917 | H | CF ₃ | Br | CF ₃ | H | H |
| | 918 | H | CF ₃ | Br | H | H | H |
| 25 | 919 | H | CF ₃ | Br | Cl | OH | H |
| | 920 | H | CF ₃ | Br | Br | OH | H |
| | 921 | H | CF ₃ | Br | I | OH | H |

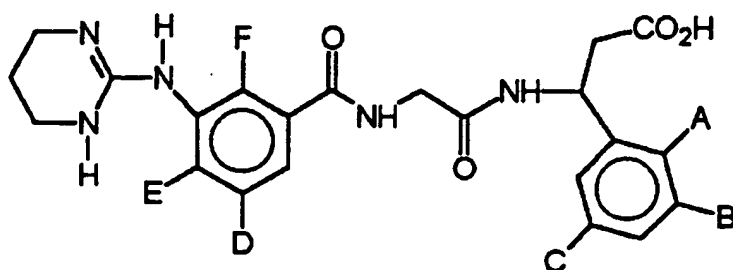
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|-----------------|----------|-----------------|-----------------|----------|
| 10 | 922 | H | CF ₃ | Br | Br | H | H |
| | 923 | H | CF ₃ | Br | OH | H | H |
| | 924 | H | CF ₃ | Br | NO ₂ | H | H |
| | 925 | H | CF ₃ | Br | I | H | H |
| | 926 | H | CF ₃ | Br | Cl | H | H |
| 15 | 927 | H | CF ₃ | Br | Cl | H | Cl |
| | 928 | H | CF ₃ | Br | OMe | H | H |
| | 929 | H | CF ₃ | Br | H | CF ₃ | H |
| | 930 | H | CF ₃ | Br | H | OH | H |
| | 931 | H | CF ₃ | Br | H | OMe | H |
| 20 | 932 | H | CF ₃ | Br | H | Cl | H |
| | 933 | H | CF ₃ | Br | H | Cl | Cl |
| | 934 | H | CF ₃ | Br | H | Br | H |
| | 935 | H | CF ₃ | Br | CF ₃ | H | H |
| | 936 | H | CF ₃ | Br | H | H | H |
| 25 | 937 | H | CF ₃ | Br | Cl | OR | H |
| | 938 | H | CF ₃ | Br | Br | OH | H |
| | 939 | H | CF ₃ | Br | I | OH | H |

- 710 -

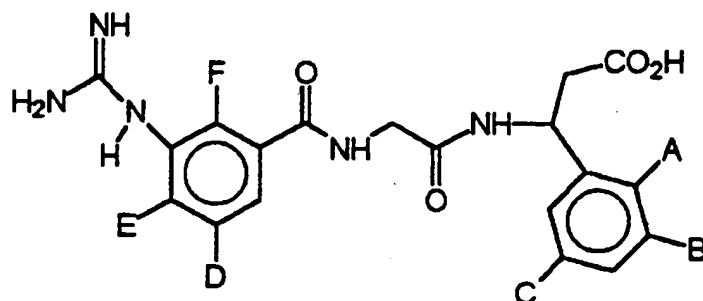
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|-----------------|----------|-----------------|-----------------|----------|
| 10 | 940 | H | CF ₃ | Br | Br | H | H |
| | 941 | H | CF ₃ | Br | OH | H | H |
| | 942 | H | CF ₃ | Br | NO ₂ | H | H |
| | 943 | H | CF ₃ | Br | I | H | H |
| | 944 | H | CF ₃ | Br | Cl | H | H |
| 15 | 945 | H | CF ₃ | Br | Cl | H | Cl |
| | 946 | H | CF ₃ | Br | OMe | H | H |
| | 947 | H | CF ₃ | Br | H | CF ₃ | H |
| | 948 | H | CF ₃ | Br | H | OH | H |
| | 949 | H | CF ₃ | Br | H | OMe | H |
| 20 | 950 | H | CF ₃ | Br | H | Cl | H |
| | 951 | H | CF ₃ | Br | H | Cl | Cl |
| | 952 | H | CF ₃ | Br | H | Br | H |
| | 953 | H | CF ₃ | Br | CF ₃ | H | H |
| | 954 | H | CF ₃ | Br | H | H | H |
| 25 | 955 | H | CF ₃ | Br | Cl | OH | H |
| | 956 | H | CF ₃ | Br | Br | OH | H |
| | 957 | H | CF ₃ | Br | I | OH | H |

- 711 -

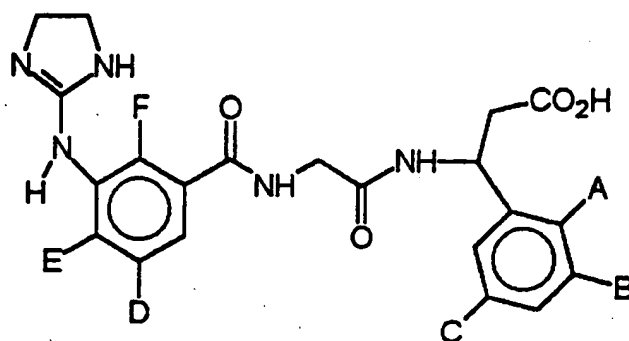
5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|-----------------|----------|-----------------|-----------------|----------|
| 10 | 958 | H | CF ₃ | I | Br | H | H |
| | 959 | H | CF ₃ | I | OH | H | H |
| | 960 | H | CF ₃ | I | NO ₂ | H | H |
| | 961 | H | CF ₃ | I | I | H | H |
| | 962 | H | CF ₃ | I | Cl | H | H |
| 15 | 963 | H | CF ₃ | I | Cl | H | Cl |
| | 964 | H | CF ₃ | I | OMe | H | H |
| | 965 | H | CF ₃ | I | H | CF ₃ | H |
| | 966 | H | CF ₃ | I | H | OH | H |
| | 967 | H | CF ₃ | I | H | OMe | H |
| 20 | 968 | H | CF ₃ | I | H | Cl | H |
| | 969 | H | CF ₃ | I | H | Cl | Cl |
| | 970 | H | CF ₃ | I | H | Br | H |
| | 971 | H | CF ₃ | I | CF ₃ | H | H |
| | 972 | H | CF ₃ | I | H | H | H |
| 25 | 973 | H | CF ₃ | I | Cl | OH | H |
| | 974 | H | CF ₃ | I | Br | OH | H |
| | 975 | H | CF ₃ | I | I | OH | H |

- 712 -

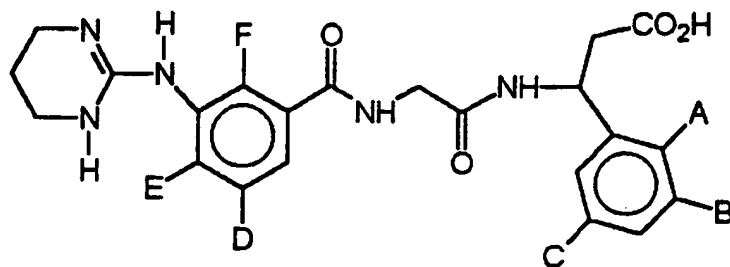
5



| <u>Example #</u> | | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|------------------|-----|----------|-----------------|----------|-----------------|-----------------|----------|
| 10 | 976 | H | CF ₃ | I | Br | H | H |
| | 977 | H | CF ₃ | I | OH | H | H |
| | 978 | H | CF ₃ | I | NO ₂ | H | H |
| | 979 | H | CF ₃ | I | I | H | H |
| | 980 | H | CF ₃ | I | Cl | H | H |
| | 981 | H | CF ₃ | I | Cl | H | Cl |
| 15 | 982 | H | CF ₃ | I | OMe | H | H |
| | 983 | H | CF ₃ | I | H | CF ₃ | H |
| | 984 | H | CF ₃ | I | H | OH | H |
| | 985 | H | CF ₃ | I | H | OMe | H |
| | 986 | H | CF ₃ | I | H | Cl | H |
| 20 | 987 | H | CF ₃ | I | H | Cl | Cl |
| | 988 | H | CF ₃ | I | H | Br | H |
| | 989 | H | CF ₃ | I | CF ₃ | H | H |
| | 990 | H | CF ₃ | I | H | H | H |
| | 991 | H | CF ₃ | I | Cl | OH | H |
| 25 | 992 | H | CF ₃ | I | Br | OH | H |
| | 993 | H | CF ₃ | I | I | OH | H |

- 713 -

5



| | <u>Example #</u> | <u>A</u> | <u>B</u> | <u>C</u> | <u>D</u> | <u>E</u> | <u>F</u> |
|----|------------------|----------|-----------------|----------|-----------------|-----------------|----------|
| 10 | 994 | H | CF ₃ | I | Br | H | H |
| | 995 | H | CF ₃ | I | OH | H | H |
| | 996 | H | CF ₃ | I | NO ₂ | H | H |
| | 997 | H | CF ₃ | I | I | H | H |
| | 998 | H | CF ₃ | I | Cl | H | H |
| 15 | 999 | H | CF ₃ | I | Cl | H | Cl |
| | 1000 | H | CF ₃ | I | OMe | H | H |
| | 1001 | H | CF ₃ | I | H | CF ₃ | H |
| | 1002 | H | CF ₃ | I | H | OH | H |
| | 1003 | H | CF ₃ | I | H | OMe | H |
| | 1004 | H | CF ₃ | I | H | Cl | H |
| 20 | 1005 | H | CF ₃ | I | H | Cl | Cl |
| | 1006 | H | CF ₃ | I | H | Br | H |
| | 1007 | H | CF ₃ | I | CF ₃ | H | H |
| | 1008 | H | CF ₃ | I | H | H | H |
| | 1009 | H | CF ₃ | I | Cl | OH | H |
| 25 | 1010 | H | CF ₃ | I | Br | OH | H |
| | 1011 | H | CF ₃ | I | I | OH | H |

- 714 -

The activity of the compounds of the present invention was tested in the following assays. The results of testing in the assays are tabulated in Table 1.

5

VITRONECTIN ADHESION ASSAY

MATERIALS

Human vitronectin receptor($\alpha_v\beta_3$) was purified from human placenta as previously described [Pytela et al.,
10 Methods in Enzymology, 144:475-489 (1987)]. Human vitronectin was purified from fresh frozen plasma as previously described [Yatohgo et al., Cell Structure and Function, 13:281-292 (1988)]. Biotinylated human vitronectin was prepared by coupling NHS-biotin from
15 Pierce Chemical Company (Rockford, IL) to purified vitronectin as previously described [Charo et al., J. Biol. Chem., 266(3):1415-1421 (1991)]. Assay buffer, OPD substrate tablets, and RIA grade BSA were obtained from Sigma (St. Louis, MO). Anti-biotin
20 antibody was obtained from Calbiochem (La Jolla, CA). Linbro microtiter plates were obtained from Flow Labs (McLean, VA). ADP reagent was obtained from Sigma (St. Louis, MO).

25 METHODS

Solid Phase Receptor Assays

This assay was essentially the same as previously reported [Niiya et al., Blood, 70:475-483 (1987)]. The
30 purified human vitronectin receptor ($\alpha_v\beta_3$) was diluted from stock solutions to 1.0 $\mu\text{g/mL}$ in Tris-buffered saline containing 1.0 mM Ca^{++} , Mg^{++} , and Mn^{++} , pH 7.4 (TBS^{+++}). The diluted receptor was immediately transferred to Linbro microtiter plates at 100 $\mu\text{L/well}$.
35 (100 ng receptor/well). The plates were sealed and incubated overnight at 4°C to allow the receptor to bind to the wells. All remaining steps were at room

- 715 -

temperatur . The assay plates were emptied and 200 μ L of 1% RIA grade BSA in TBS⁺⁺⁺ (TBS⁺⁺⁺/BSA) were added to block exposed plastic surfaces. Following a 2 hour incubation, the assay plates were washed with TBS⁺⁺⁺ using a 96 well plate washer. Logarithmic serial dilution of the test compound and controls were made starting at a stock concentration of 2 mM and using 2 nM biotinylated vitronectin in TBS⁺⁺⁺/BSA as the diluent. This premixing of labeled ligand with test (or control) ligand, and subsequent transfer of 50 μ L aliquots to the assay plate was carried out with a CETUS Propette robot; the final concentration of the labeled ligand was 1 nM and the highest concentration of test compound was 1.0×10^{-4} M. The competition occurred for two hours after which all wells were washed with a plate washer as before. Affinity purified horseradish peroxidase labeled goat anti-biotin antibody was diluted 1:3000 in TBS⁺⁺⁺/BSA and 125 μ L were added to each well. After 30 minutes, the plates were washed and incubated with OPD/H₂O₂ substrate in 100 mM/L Citrate buffer, pH 5.0. The plate was read with a microtiter plate reader at a wavelength of 450 nm and when the maximum-binding control wells reached an absorbance of about 1.0, the final A₄₅₀ were recorded for analysis. The data were analyzed using a macro written for use with the EXCEL™ spreadsheet program. The mean, standard deviation, and %CV were determined for duplicate concentrations. The mean A₄₅₀ values were normalized to the mean of four maximum-binding controls (no competitor added) (B-MAX). The normalized values were subjected to a four parameter curve fit algorithm [Rodbard et al., Int. Atomic Energy Agency, Vienna, pp 469 (1977)], plotted on a semi-log scale, and the computed concentration corresponding to inhibition of 50% of the maximum binding of biotinylated vitronectin (IC₅₀) and corresponding R² was reported for those compounds exhibiting greater than 50% inhibition at the

- 716 -

highest concentration tested; otherwise the IC_{50} is reported as being greater than the highest concentration tested. β -[[2-[[5-[(aminoiminomethyl)amino]-1-oxopentyl]amino]-1-oxoethyl]amino]-3-pyridinepropanoic acid [USSN 08/375,338, Example 1] which is a potent α,β antagonist (IC_{50} in the range 3-10 nM) was included on each plate as a positive control.

10

PURIFIED IIb/IIIa RECEPTOR ASSAY

MATERIALS

Human fibrinogen receptor ($\alpha_{IIb}\beta_3$) was purified from outdated platelets. (Pytela, R., Pierschbacher, M.D., Argraves, S., Suzuki, S., and Rouslahti, E. "Arginine-Glycine-Aspartic acid adhesion receptors", Methods in Enzymology 144(1987):475-489.) Human vitronectin was purified from fresh frozen plasma as described in Yatohgo, T., Izumi, M., Kashiwagi, H., and Hayashi, M., "Novel purification of vitronectin from human plasma by heparin affinity chromatography," Cell Structure and Function 13(1988):281-292. Biotinylated human vitronectin was prepared by coupling NHS-biotin from Pierce Chemical Company (Rockford, IL) to purified vitronectin as previously described. (Charo, I.F., Nannizzi, L., Phillips, D.R., Hsu, M.A., Scarborough, R.M., "Inhibition of fibrinogen binding to GP IIb/IIIa by a GP IIIa peptide", J. Biol. Chem. 266(3)(1991): 1415-1421.) Assay buffer, OPD substrate tablets, and RIA grade BSA were obtained from Sigma (St. Louis, MO). Anti-biotin antibody was obtained from Calbiochem (La Jolla, CA). Linbro microtiter plates were obtained from Flow Labs (McLean, VA). ADP reagent was obtained from Sigma (St. Louis, MO).

35

- 717 -

METHODSSolid Phase Receptor Assays

This assay is essentially the same reported in Niiya, K., Hodson, E., Bader, R., Byers-Ward, V. Koziol, J.A., Plow, E.F. and Ruggeri, Z.M., "Increased surface expression of the membrane glycoprotein IIb/IIIa complex induced by platelet activation: Relationships to the binding of fibrinogen and platelet aggregation", Blood 70(1987):475-483. The purified human fibrinogen receptor ($\alpha_{IIb}\beta_3$) was diluted from stock solutions to 1.0 $\mu\text{g/mL}$ in Tris-buffered saline containing 1.0 mM Ca^{++} , Mg^{++} , and Mn^{++} , pH 7.4 (TBS^{+++}). The diluted receptor was immediately transferred to Linbro microtiter plates at 100 $\mu\text{L/well}$ (100 ng receptor/well). The plates were sealed and incubated overnight at 4°C to allow the receptor to bind to the wells. All remaining steps were at room temperature. The assay plates were emptied and 200 μL of 1% RIA grade BSA in TBS^{+++} ($\text{TBS}^{+++}/\text{BSA}$) were added to block exposed plastic surfaces. Following a 2 hour incubation, the assay plates were washed with TBS^{+++} using a 96 well plate washer. Logarithmic serial dilution of the test compound and controls were made starting at a stock concentration of 2 mM and using 2 nM biotinylated vitronectin in $\text{TBS}^{+++}/\text{BSA}$ as the diluent. This premixing of labeled ligand with test (or control) ligand, and subsequent transfer of 50 μL aliquots to the assay plate was carried out with a CETUS Propette robot; the final concentration of the labeled ligand was 1 nM and the highest concentration of test compound was 1.0×10^{-4} M. The competition occurred for two hours after which all wells were washed with a plate washer as before. Affinity purified hors radish peroxidase labeled goat anti-biotin antibody was diluted 1:3000 in $\text{TBS}^{+++}/\text{BSA}$ and 125 μL were added to each well. After 30 minutes, the

- 718 -

plates were washed and incubated with ODD/H₂O₂ substrate in 100 mM/L citrate buffer, pH 5.0. The plate was read with a microtiter plate reader at a wavelength of 450 nm and when the maximum-binding control wells reached an absorbance of about 1.0, the final A₄₅₀ were recorded for analysis. The data were analyzed using a macro written for use with the EXCEL™ spreadsheet program. The mean, standard deviation, and %CV were determined for duplicate concentrations. The mean A₄₅₀ values were normalized to the mean of four maximum-binding controls (no competitor added) (B-MAX). The normalized values were subjected to a four parameter curve fit algorithm, [Robard et al., Int. Atomic Energy Agency, Vienna, pp 469 (1977)], plotted on a semi-log scale, and the computed concentration corresponding to inhibition of 50% of the maximum binding of biotinylated vitronectin (IC₅₀) and corresponding R² was reported for those compounds exhibiting greater than 50% inhibition at the highest concentration tested; otherwise the IC₅₀ is reported as being greater than the highest concentration tested. β -[[2-[[5-[(aminoiminomethyl)amino]-1-oxopentyl]amino]-1-oxoethyl]amino]-3-pyridinepropanoic acid [USSN 08/375,338, Example 1] which is a potent α,β , antagonist (IC₅₀ in the range 3-10 nM) was included on each plate as a positive control.

Human Platelet Rich Plasma Assays

Healthy aspirin free donors were selected from a pool of volunteers. The harvesting of platelet rich plasma and subsequent ADP induced platelet aggregation assays were performed as described in Zucker, M.B., "Platelet Aggregation Measured by the Photometric Method", Methods in Enzymology 169(1989):117-133. Standard venipuncture techniques using a butterfly allowed the withdrawal of 45 mL of whole blood into a 60 mL syringe containing 5 mL of 3.8% trisodium

- 719 -

citrate. Following thorough mixing in the syringe, the anti-coagulated whole blood was transferred to a 50 mL conical polyethylene tube. The blood was centrifuged at room temperature for 12 minutes at 200 xg to sediment non-platelet cells. Platelet rich plasma was removed to a polyethylene tube and stored at room temperature until used. Platelet poor plasma was obtained from a second centrifugation of the remaining blood at 2000 xg for 15 minutes. Platelet counts are typically 300,000 to 500,000 per microliter. Platelet rich plasma (0.45 mL) was aliquoted into siliconized cuvettes and stirred (1100 rpm) at 37°C for 1 minute prior to adding 50 uL of pre-diluted test compound. After 1 minute of mixing, aggregation was initiated by the addition of 50 uL of 200 uM ADP. Aggregation was recorded for 3 minutes in a Payton dual channel aggregometer (Payton Scientific, Buffalo, NY). The percent inhibition of maximal response (saline control) for a series of test compound dilutions was used to determine a dose response curve. All compounds were tested in duplicate and the concentration of half-maximal inhibition (IC_{50}) was calculated graphically from the dose response curve for those compounds which exhibited 50% or greater inhibition at the highest concentration tested; otherwise, the IC_{50} is reported as being greater than the highest concentration tested.

M21 MELANOMA CELL ADHESION ASSAY

This assay involves an $\alpha_v\beta_3$ -dependent adhesion of M21 human melanoma cells to human fibrinogen-coated plastic tissue culture dishes.

Fibrinogen was purified from human plasma. Fibronectin and plasminogen were eliminated from the preparation by passing the sample over gelatin-sepharose 4B and lysine-sepharose 4B resins,

- 720 -

- respectively. The fibrinogen is diluted to 10 $\mu\text{g/mL}$ in coating buffer (20 mM Tris-HCl, 150 mM NaCl, pH 7.4). 100 μL of diluted fibrinogen is added to each well of a 96-well Immulon 2 microtiter plate (Dynatech; Chantilly, Va) and allowed to coat overnight at 4°C. Plates are blocked with 1% BSA (Miles/Pentex; Kankakee, IL) in adhesion buffer (Hank's balanced salt solution without Ca^{++} or Mg^{++} [HBSS--], 50 mM Hepes, 1 mg/mL BSA, pH 7.4) for 1 hour at 37°C.
- 10 M21 human melanoma cells were provided by Dr. J. Smith, La Jolla Cancer Research Institute. M21 cells are harvested from tissue culture flasks by washing with HBSS-- and adding cell dissociation solution (Sigma) and incubating for 5 minutes at 37°C.
- 15 Harvested cells are washed 3 times with adhesion assay buffer containing 200 μM Mn^{++} . Cells are counted and suspended to a density of $2 \times 10^6/\text{mL}$ in adhesion assay buffer containing 200 μM Mn^{++} . M21 cells are pre-incubated with antagonists of $\alpha_v\beta_3$ for 30 minutes at room temperature. Following the pre-incubation, the solutions containing a mixture of cells and antagonists are added to each well of the microtiter plate and allowed to bind for 30 minutes at 37°C.
- 20 Following adhesion, plates are gently washed 3 times with 200 μL of wash buffer (50 mM Tris-HCl, 150 mM NaCl, pH 7.4) using large bore pipet tips. Plates are briefly blotted dry and 100 μL of cell lysis buffer (50 mM sodium acetate, pH 5.0, 0.5% Triton X-100, 0.3 mg/mL p-nitrophenyl phosphate [Sigma] is added to each well. Plates are incubated for 60 minutes at 37°C and 50 μL of 1N NaOH is added to stop the reaction. The absorbance of the wells at 412 nm is read using an automatic plate reader.
- 30

- 721 -

TABLE I

| Example | AvB3 IC50 (nM) | IIB/IIIA IC50 (nM) | M21 Melanoma Cells IC 50 (nM) | Human PRP (μ M) |
|--------------|----------------------|--------------------------|-------------------------------------|-------------------------|
| 1 | 76.9 | 8350 | | > 200 |
| 2 | 0.54 | 51.2 | 0.25 | 200 |
| 3 | 498 | 72900 | 3050 | |
| 4 | 3.17 | 473 | 3.3 | > 200 |
| 5 | 227 | 3150 | | |
| 6 | 1.04 | 15.9 | | 80 |
| 8 | 0.69 | 9.83 | 0.28 | 73.3 |
| 10 | 0.92 | 54.4 | 1.82 | > 200 |
| 12 | 1.1 | 595 | 9.32 | > 200 |
| 14 | 1.62 | 139 | 5.42 | > 200 |
| 15 | 10.2 | 3830 | 202 | > 200 |
| 17 | 2.66 | 137 | 3.64 | > 200 |
| 19 | 303 | 72000 | | |
| 21 | 2.44 | 1910 | | > 200 |
| 22 | 1.37 | 280 | | > 200 |
| 24 | 0.91 | 58.6 | 12.7 | > 200 |
| 26 | 14.2 | 809 | | > 200 |
| 27 | 1.53 | 178 | | > 200 |
| 30 | 1.75 | 424 | 320 | > 200 |
| 34 | 94.3 | 269 | | > 200 |
| 35 | 57.1 | 6.21 | | 69.5 |
| 36 Step B | 14.6 | 1580 | 143 | > 200 |
| 37 | 0.88 | 13.9 | | > 20.0 |
| 39 | 12.2 | 1540 | | > 20.0 |
| 40 | 10.3 | 834 | | > 200 |
| 41 | 12.1 | 830 | | > 200 |
| 42 | 124 | 9800 | | |
| 43 | 28.3 | 1640 | 188 | > 200 |
| 44 | 0.33 | 998 | | > 20.0 |
| 45 | 0.69 | 39.5 | 2.54 | 167 |

- 722 -

| Example | AvB3 IC50 (nM) | IIb/IIIa IC50 (nM) | M21 Melanoma Cells IC 50 (nM) | Human PRP (μ M) |
|---------|----------------------|--------------------------|-------------------------------------|-------------------------|
| 46 | 5.34 | 1680 | 147 | > 200 |
| 47 | 0.86 | 4270 | 1.18 | > 200 |
| 51 | 9730 | >100000 | | |
| 52 | 3.62 | 139 | 11.7 | > 200 |
| 53 | 54.6 | 930 | | > 200 |
| 54 | 10.7 | 175 | | > 200 |
| 55 | 4.77 | 117 | | > 200 |
| 56 | 3.12 | 65.3 | 6.87 | > 200 |
| 57 | 1340 | 15300 | | |
| 58 | 162 | 5740 | | |
| 59 | 2.35 | 172 | 24.3 | > 200 |
| 60 (B) | 1.21 | 72.7 | | > 200 |
| 60 (C) | 0.73 | 16.4 | 0.74 | > 200 |
| 61 | 1.76 | 192 | 228 | > 200 |
| 62 | 1.42 | 28.4 | | > 200 |
| 65 | 9.7 | 170 | 13.8 | > 200 |
| 66 | 1.44 | 73.7 | 2.51 | > 100 |
| 67 | 2.05 | 92.3 | 4.08 | > 200 |
| 68 | 5.48 | 125 | | > 200 |
| 69 | 0.92 | 33.6 | 0.95 | > 200 |
| 70 | 63 | 3240 | 924 | > 200 |
| 71 | 20.4 | 202 | 1040 | > 200 |
| 72 | 1.21 | 152 | | > 200 |
| 80 | 9.49 | 4.35 | | 30 |
| 82 | 334 | 353 | | |
| 83 | 3.39 | 97.7 | 11 | > 200 |
| 84 | 2800 | 246 | | |
| 85 | 6.65 | 8.07 | | |
| 86 | 8.79 | 246 | | > 200 |
| 87 | 6.35 | 732 | | > 200 |
| 88 | 8.44 | 945 | 52.3 | > 200 |

- 723 -

| Exempl | AvB3 IC50 (nM) | IIb/IIIa IC50 (nM) | M21 Melanoma Cells IC 50 (nM) | Human PRP (μ M) |
|--------|----------------------|--------------------------|-------------------------------------|-------------------------|
| 89 | 1240 | 9830 | | |
| 94 | 1.16 | 101 | 1 | > 200 |
| 95 | 1.43 | 25.4 | | > 200 |
| 96 | 1810 | 5400 | | |
| 97 | 26.9 | 1170 | 163 | |
| 98 | 146 | 500 | | |
| 99 | 0.38 | 1.89 | 0.49 | 57.5 |
| 100 | 8560 | >100000 | | |
| 101 | 1680 | 65700 | | |
| 103 | 16.6 | 19100 | | > 20.0 |
| 106 | 0.79 | 3140 | 0.81 | > 200 |
| 107 | 6400 | 18700 | | |
| 108 | 25.2 | 4870 | | > 200 |
| 109 | 575 | >100000 | | |
| 110 | 4.5 | 1860 | 177 | > 200 |
| 112 | 284 | 6340 | | |
| 113 | 276 | 100000 | | |
| 114 | 3.26 | 2940 | 200 | > 200 |
| 116 | 15500 | >100000 | | |
| 117 | 60.1 | 20100 | | > 200 |
| 119 | 3.61 | 11100 | 90.4 | > 20.0 |
| 121 | 2840 | >100000 | | |
| 122 | 0.79 | 420 | | > 20.0 |
| 123 | 11800 | 85500 | | |
| 124 | 22 | 317 | | > 20.0 |
| 126 | 2.48 | 2010 | | > 200 |
| 127 | 0.51 | 461 | | > 200 |
| 129 | 68.9 | 9460 | | > 200 |
| 130 | 47 | 2690 | | > 200 |
| 131 | 3.82 | 1760 | | > 20.0 |
| 135 | 50700 | >100000 | | |

- 724 -

| Example | AvB3 IC50 (nM) | I Ib/IIIa IC50 (nM) | M21 Melanoma Cells IC 50 (nM) | Human PRP (μ M) |
|---------|----------------------|---------------------------|-------------------------------------|-------------------------|
| 136 | 54.4 | 14200 | | > 20.0 |
| 137 | 16.2 | 6500 | | > 200 |
| 138 | 36.9 | 5820 | | > 200 |
| 139 | 23.8 | 16100 | | > 200 |
| 140 | 4590 | >100000 | | |
| 141 | 3.09 | 125 | | > 200 |
| 143 | 6700 | >100000 | | |
| 144 | 55.3 | 5830 | | > 200 |
| 145 | 2720 | >100000 | | |
| 146 | 14.3 | 879 | | > 200 |
| 150 | 5.74 | 631 | | > 200 |
| 155 | 5.05 | 81.1 | | > 200 |
| 158 | 10.1 | 547 | | |
| 160 | 25.6 | 10400 | | |
| 162 | 4.62 | 1340 | | >200 |
| 166 | 13000 | 45900 | | |
| 168 | 2.29 | 269 | | |
| 171 | 0.35 | 83.2 | | |
| 173 | 0.5 | 17.4 | | |
| 175 | 2.12 | 205 | | |
| 177 | 0.58 | 137 | | >20.0 |
| 179 | 2.72 | 927 | | |
| 181 | 132 | 22800 | | |
| 183 | 1.58 | 258 | | |
| 185 | 1.47 | 166 | | |
| 187 | 1.31 | 264 | | |
| 189 | 4.03 | 1980 | | |
| 191 | 0.49 | 70.3 | | >20.0 |
| 193 | 2.56 | 209 | | >20.0 |
| 195 | 1.09 | 98 | | |
| 198 | 114 | 37800 | | |
| 200 | 0.48 | 1100 | | >200 |

- 725 -

| Example | AvB3 IC50 (nM) | IIb/IIIa IC50 (nM) | M21 Melanoma Cells IC 50 (nM) | Human PRP (μ M) |
|---------|----------------------|--------------------------|-------------------------------------|-------------------------|
| 201 | 58.1 | 10800 | | |
| 203 | 3.56 | 650 | | |
| 205 | 1.68 | 1240 | | |
| 206 | 78.5 | 22000 | | |
| 207 | 0.9 | 148 | | |
| 208 | 1.15 | 277 | | |
| 209 | 0.83 | 140 | | |
| 210 | 2.62 | 343 | | |
| 211 | 0.47 | 607 | | |
| 212 | 1.93 | 306 | | |
| 213 | 2.93 | 334 | | |
| 214 | 2.35 | 454 | | |
| 215 | 0.41 | 656 | | |
| 216 | 1 | 326 | | |
| 217 | 74.8 | 78900 | | |
| 219 | 2.29 | 253 | | |
| 221 | 70.5 | 23.7 | | >200 |
| 222 | 2.02 | 112 | | >200 |
| 223 | 4.36 | 293 | | >200 |
| 224 | 0.71 | 25.9 | | |
| 225 | 2.76 | 471 | | >20.0 |
| 226 | 7.07 | 2910 | | >200 |
| 227 | 14.1 | 2640 | | >200 |
| 228 | 3.36 | 583 | | >200 |
| 229 | 39.1 | 10600 | | |
| 231 | 2.99 | 424 | | |
| 232 | 19.1 | 12100 | | >200 |
| 233 | 3.31 | 647 | | >200 |
| 234 | 89.3 | 830 | | |
| 235 | 0.54 | 29.9 | | |
| 236 | 0.53 | 1250 | | |
| 237 | 0.57 | 1950 | | |
| 238 | 0.92 | 646 | | |

- 726 -

| Example | AvB3 IC50 (nM) | IIb/IIIa IC50 (nM) | M21 Melanoma Cells IC 50 (nM) | Human PRP (μ M) |
|---------|----------------------|--------------------------|-------------------------------------|-------------------------|
| 239 | 0.83 | 673 | | |
| 240 | 49400 | 76400 | | |
| 241 | 557 | 17200 | | |
| 242 | 2.28 | 533 | | |
| 243 | 0.35 | 23.6 | | |
| 244 | 17.6 | 4560 | | |
| 245 | 0.96 | 134 | | |
| 246 | 7.24 | 802 | | |
| 247 | 1.24 | 417 | | |
| 248 | 12300 | 21000 | | |
| 249 | 5.31 | 244 | | |
| 251(B) | 3.49 | 280 | | |
| 251(C) | 0.76 | 124 | | |
| 252 | 1.52 | 213 | | |
| 253 | 0.84 | 109 | | |
| 254 | 16.5 | 6910 | | |
| 255 | 28.4 | 6050 | | |
| 256 | 0.58 | 22 | | |
| 257 | 49.2 | 4660 | | |
| 259 | 0.81 | 86.7 | | |
| 260 | 0.74 | 65.3 | | |
| 261 | 6.47 | 4710 | | |
| 262 | 1.24 | 172 | | |
| 263 | 4.19 | 2760 | | |
| 264 | 2.18 | 574 | | |
| 265 | 6.19 | 706 | | |
| 266 | 0.77 | 1810 | | |
| 267 | 131 | 43900 | | |
| 268 | 0.67 | 7430 | | |
| 269 | 209 | 25400 | | |
| 270 | 5.51 | 9160 | | |
| 271 | 29.9 | 4610 | | |
| 272 | 893 | 8210 | | |

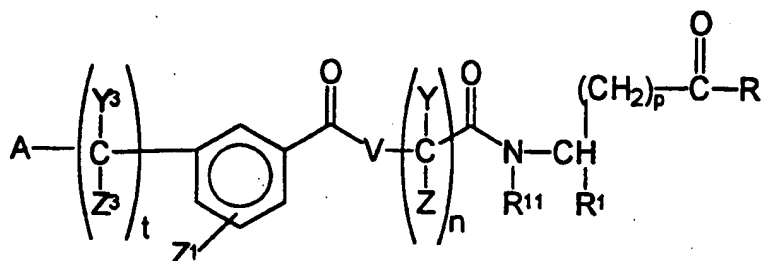
- 727 -

| Example | AvB3 IC50 (nM) | IIb/IIIa IC50 (nM) | M21 Melanoma Cells IC 50 (nM) | Human PRP (μ M) |
|---------|----------------------|--------------------------|-------------------------------------|-------------------------|
| 273 | 12.9 | 4160 | | |
| 274 | 31.1 | 21200 | | |
| 275 | 6.98 | 1200 | | |
| 276 | 1.25 | 111 | | |
| 277 | 1.41 | 198 | | |
| 278 | 0.45 | 150 | | |
| 279 | 7.12 | 637 | | |
| 281 | 4.16 | 11500 | | |
| 282 | 864 | 9770 | | |
| 284 | 195 | 18400 | | |
| 285 | 229 | 3170 | | |
| 286 | 413 | 8090 | | |
| 287 | 49.7 | 41.1 | | |
| 288 | 8.62 | 1060 | | |
| 289 | 0.9 | 621 | | |
| 290 | 1.62 | 1020 | | |
| 291 | 1.24 | 37.4 | | |
| 292 | 3.55 | 337 | | |
| 294 | 173 | 1990 | | |
| 295 | 144 | 4560 | | |
| 296 | 404 | 9450 | | |
| 297 | 89.8 | 3920 | | |
| 298 | 252 | 5560 | | |
| 299 | 109 | 927 | | |
| 362 | 0.84 | 7260 | | |
| 363 | 2.12 | 509 | | |
| 364 | 3.58 | 223 | | |
| 365 | 16.9 | 8470 | | |
| 366 | 0.44 | 91.3 | | |
| 367 | 0.35 | 1540 | | |

- 728 -

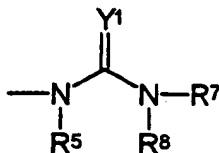
What is claimed is:

1. A compound of the formula



or a pharmaceutically acceptable salt thereof,
wherein

A is



wherein Y¹ is selected from the group consisting of
N-R², O, and S;

R² is selected from the group consisting of H;
alkyl; aryl; hydroxy; alkoxy; cyano; nitro; amino;
alkenyl; alkynyl; amido; alkylcarbonyl;
arylcabonyl; alkoxycarbonyl; aryloxy carbonyl;
haloalkylcarbonyl; haloalkoxycarbonyl;
alkylthiocarbonyl; arylthiocarbonyl;
acyloxymethoxycarbonyl; alkyl optionally
substituted with one or more substituent selected
from lower alkyl, halogen, hydroxyl, haloalkyl,
cyano, nitro, carboxyl, amino, alkoxy, aryl or
aryl optionally substituted with one or more
halogen, haloalkyl, lower alkyl, alkoxy, cyano,
alkylsulfonyl, alkylthio, nitro, carboxyl, amino,
hydroxyl, sulfonic acid, sulfonamide, aryl, fused
aryl, monocyclic heterocycles, or fused mon cyclic

- 729 -

heterocycles; aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, hydroxy, lower alkyl, alkoxy, methylenedioxy, ethylenedioxy, cyano, nitro, alkylthio, alkylsulfonyl, sulfonic acid, sulfonamide, carboxyl derivatives, amino, aryl, fused aryl, monocyclic heterocycles and fused monocyclic heterocycle; monocyclic heterocycles; and monocyclic heterocycles optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, amino, nitro, hydroxy, carboxyl derivatives, cyano, alkylthio, alkylsulfonyl, sulfonic acid, sulfonamide, aryl or fused aryl; or

R² taken together with R⁷ forms a 4-12 membered dinitrogen containing heterocycle optionally substituted with one or more substituent selected from the group consisting of lower alkyl, hydroxy, keto, alkoxy, halo, phenyl, amino, carboxyl or carboxyl ester, and fused phenyl;

or R² taken together with R⁷ forms a 5 membered heteroaromatic ring optionally substituted with one or more substituent selected from lower alkyl, phenyl and hydroxy;

or R² taken together with R⁷ forms a 5 membered heteroaromatic ring fused with a phenyl group;

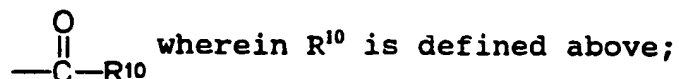
R⁷ (when not taken together with R²) and R⁸ are independently selected from the group consisting of H; alkyl; alkenyl; alkynyl; aralkyl; amino; alkylamino; hydroxy; alkoxy; arylamino; amido, alkylcarbonyl, arylcarbonyl; alkoxycarbonyl; aryloxy carbonyl; haloalkylcarbonyl; aryloxy; haloalkoxycarbonyl; alkylthiocarbonyl;

- 730 -

arylthiocarbonyl; acyloxymethoxycarbonyl; cycloalkyl; bicycloalkyl; aryl; acyl; benzoyl; alkyl optionally substituted with one or more substituent selected from lower alkyl, halogen, hydroxy, haloalkyl, cyano, nitro, carboxyl derivatives, amino, alkoxy, thio, alkylthio, sulfonyl, aryl, aralkyl, aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, carboxyl derivatives, aryloxy, amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethyl, sulfonyl, alkylsulfonyl, haloalkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles, fused monocyclic heterocycles; aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, carboxyl derivatives, aryloxy, amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethylsulfonyl, alkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles, or fused monocyclic heterocycles; monocyclic heterocycles; monocyclic heterocycles optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, aryloxy, amino, nitro, hydroxy, carboxyl derivatives, cyano, alkylthio, alkylsulfonyl, aryl, fused aryl; monocyclic and bicyclic heterocyclicalkyls; $-SO_2R^{10}$ wherein R^{10} is selected from the group consisting of alkyl, aryl and monocyclic heterocycles, all optionally substituted with one or more substituent selected from the group consisting of halogen, haloalkyl,

- 731 -

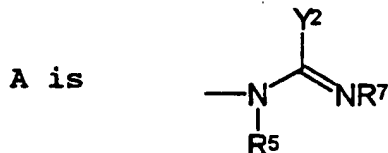
alkyl, alkoxy, cyano, nitro, amino, acylamino, trifluoroalkyl, amido, alkylaminosulfonyl, alkylsulfonyl, alkylsulfonylamino, alkylamino, dialkylamino, trifluoromethylthio, trifluoroalkoxy, trifluoromethylsulfonyl, aryl, aryloxy, thio, alkylthio, and monocyclic heterocycles; and



or NR^7 and R^8 taken together form a 4-12 membered mononitrogen containing monocyclic or bicyclic ring optionally substituted with one or more substituent selected from lower alkyl, carboxyl derivatives, aryl or hydroxy and wherein said ring optionally contains a heteroatom selected from the group consisting of O, N and S;

R^5 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, benzyl, and phenethyl;

or



wherein Y^2 is selected from the group consisting of alkyl; cycloalkyl; bicycloalkyl; aryl; monocyclic heterocycles; alkyl optionally substituted with aryl which can also be optionally substituted with one or more substituent selected from halo, haloalkyl, alkyl, nitro, hydroxy, alkoxy, aryloxy, aryl, or fused aryl; aryl optionally substituted

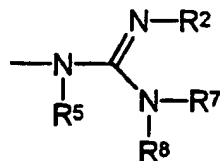
- 732 -

with one or more substituent selected from halo, haloalkyl, hydroxy, alkoxy, aryloxy, aryl, fused aryl, nitro, methylenedioxy, ethylenedioxy, or alkyl; alkynyl; alkenyl; $-S-R^9$ and $-O-R^9$ wherein R^9 is selected from the group consisting of H; alkyl; aralkyl; aryl; alkenyl; and alkynyl; or R^9 taken together with R^7 forms a 4-12 membered mononitrogen and monosulfur or monooxygen containing heterocyclic ring optionally substituted with lower alkyl, hydroxy, keto, phenyl, carboxyl or carboxyl ester, and fused phenyl; or R^9 taken together with R^7 is thiazole; oxazole; benzoxazole; or benzothiazole; and

R^5 and R^7 are as defined above;

or Y^2 (when Y^2 is carbon) taken together with R^7 forms a 4-12 membered mononitrogen containing ring optionally substituted with alkyl, aryl or hydroxy;

or A is

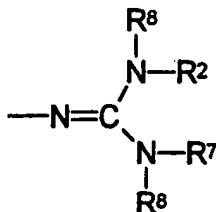


where R^2 and R^7 taken together form a 5-8 membered dinitrogen containing heterocycle optionally substituted with one or more substituent selected from the group consisting of lower alkyl, hydroxy, keto, phenyl, or carboxyl derivatives; and R^8 is selected from the group consisting of alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxy carbonyl, haloalkylcarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl, or acyloxymethoxycarbonyl; and

- 733 -

R⁵ is defined as above

or A is



where R² and R⁷ taken together form a 5-8 membered dinitrogen containing heterocycle optionally substituted with hydroxy, keto, phenyl, or alkyl; and

R⁸ are both selected from the group consisting of alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxy, haloalkylcarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl and acyloxymethoxycarbonyl;

Z¹ is one or more substituent selected from the group consisting of H; alkyl; hydroxy; alkoxy; aryloxy; halogen; haloalkyl; haloalkoxy; nitro; amino; alkylamino; acylamino; dialkylamino; cyano; alkylthio; alkylsulfonyl; carboxyl derivatives; trihaloacetamide; acetamide; aryl; fused aryl; cycloalkyl; thio; monocyclic heterocycles; fused monocyclic heterocycles; and A, wherein A is defined above;

V is selected from the group consisting of -N-(R⁶)- wherein R⁶ is selected from the group consisting of H; lower alkyl; cycloalkyl; aralkyl; aryl; and monocyclic heterocycles; or R⁶ taken together with Y, forms a 4-12 membered mononitrogen containing ring;

- 734 -

Y, Y³, Z and Z³ are independently selected from the group consisting of hydrogen; alkyl; aryl; and cycloalkyl; or Y and Z taken together form a cycloalkyl; or Y³ and Z³ taken together form a cycloalkyl;

n is an integer 1, 2, or 3;

t is an integer 0, 1, or 2;

p is an integer 0, 1, 2, or 3;

R is X-R³ wherein X is selected from the group consisting of O, S and NR⁴, wherein R³ and R⁴ are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; haloalkyl; aryl; arylalkyl; sugars; steroids; polyalkylethers; alkylamido; alkyl N,N-dialkylamido; pivaloyloxymethyl; and in the case of the free acid, all pharmaceutically acceptable salts thereof;

R¹ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; carboxyl derivatives; haloalkyl; monocyclic heterocycles; monocyclic heterocycles optionally substituted with alkyl, halogen, haloalkyl, cyano, hydroxy, aryl, fused aryl, nitro, alkoxy, aryloxy, alkylsulfonyl, arylsulfonyl, sulfonamide, thio, alkylthio, carboxyl derivatives, amino, amido;

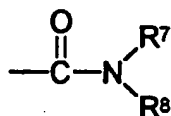
alkyl optionally substituted with one or more of halo, haloalkyl, hydroxy, alkoxy, aryloxy, thio, alkylthio, alkynyl, alkenyl, alkyl, arylthio, alkylsulfoxide, alkylsulfonyl, arylsulfoxide, arylsulfonyl, cyano, nitro, amino, alkylamino, dialkylamino, alkylsulfonamide, arylsulfonamide,

- 735 -

acylamide, carboxyl derivatives, sulfonamide, sulfonic acid, phosphonic acid derivatives, phosphinic acid derivatives, aryl, arylthio, arylsulfoxide, or arylsulfone all optionally substituted on the aryl ring with halo, alkyl, haloalkyl, cyano, nitro, hydroxy, carboxyl derivatives, alkoxy, aryloxy, amino, alkylamino, dialkylamino, amido, aryl, fused aryl, monocyclic heterocycles; and fused monocyclic heterocycles, monocyclic heterocyclicthio, monocyclic heterocyclicsulfoxide, and monocyclic heterocyclic sulfone, which can be optionally substituted with halo, haloalkyl, nitro, hydroxy, alkoxy, fused aryl, or alkyl;

alkylcarbonyl, haloalkylcarbonyl, and arylcarbonyl;

aryl optionally substituted in one or more positions with halo, haloalkyl, alkyl, alkoxy, aryloxy, methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, acyloxy, carboxyl derivatives, carboxyalkoxy, amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethylsulfonyl, alkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles and fused monocyclic heterocycles; and



wherein R⁷ and R⁸ are as defined above

and provided that taken together with the nitrogens, R⁷ and R⁸ comprise an amino acid;

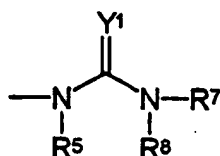
and

- 736 -

R¹¹ is selected from the group consisting of H, alkyl, aralkyl, alkenyl, alkynyl, haloalkyl or haloalkynyl or R¹¹ taken together with Y forms a 4-12 membered mononitrogen containing ring.

2. A compound according to the formula of Claim 1 wherein

A is



wherein Y¹ is selected from the group consisting of N-R², O, and S;

R² is selected from the group consisting of H, cyano, alkyl, aryl, substituted alkyl, hydroxy, alkoxy, alkylcarbonyl, amido, nitro, amino and monocyclic heterocycles, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl, acyloxymethoxycarbonyl; or R² taken together with R⁷ forms a 4-12 membered ring;

R⁵, R⁷, R⁸ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, bicycloalkyl substituted alkyl, arylalkyl, aryloxy, hydroxy, alkoxy, amino, alkylamino, arylamino, amido, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkylcarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl, acyloxymethoxycarbonyl, substituted phenyl,

- 737 -

arylacyl, monocyclic and bicyclic heterocycles, monocyclic and bicyclic heterocyclicalkyl and -SO₂R¹⁰ wherein R¹⁰ is selected from the group consisting of alkyl, amino and aryl which are all optionally substituted with one or more substituent selected from the group consisting of acylamino, amino, carbonyl, cyano, nitro, alkoxy, halo, alkyl, trifluoroalkyl, amido, alkylaminosulfonyl, alkylsulfonyl, alkylsulfonylamino, alkylamino, dialkylamino, aryloxy, thio, trifluoromethylthio, trifluoroalkoxy, and trifluoromethylsulfonyl or -NR⁷ and R⁸ taken together form a 4-12 membered ring wherein said ring optionally contains a heteroatom selected from the group consisting of O, N, and S wherein said ring is optionally substituted;

3. A compound according to Claim 2 wherein

V is -N(R⁶)- wherein R⁶ is selected from the group consisting of H and lower alkyl;

n is 1;

t is 0 or 1;

p is 0, 1 or 2; and

R is O-R³.

4. A compound according to Claim 3 selected from the group consisting of

(±)ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]pyridine-3-propanoate;

- 738 -

(±)β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]pyridine-3-
propanoic acid;

(±)ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]benzenepropanoate;

(±)β-[[2-[[[3-
[(aminoiminomethyl)amino]phenyl]carbonyl]-
amino]acetyl]amino]benzenepropanoic acid;

(±)ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-1,3-
benzodioxole-5-propanoate;

(±)β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-1,3-
benzodioxole-5-propanoic acid;

(±)ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]-
naphthalen-1-yl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoate;

(±)β-[[2-[[[3-[(aminoiminomethyl)-amino]-
naphthalen-1-yl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

(±) ethyl β-[[1-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]-1-cyclopropyl]-
carbonyl]amino]pyridine-3-propanoate;

(±) β-[[1-[[[3[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]cycloprop-1-yl]carbonyl]-
amino]pyridine-3-propanoic acid;

- 739 -

(±) thyl β -[[2-[[[3-[[imino[(phenylmethyl)amino]-methyl]amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

(±) β -[[2-[[[3-[[imino[(phenylmethyl)amino]methyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

3S-[[2-[[[3-(aminocarbonylamino)phenyl]-carbonyl]amino]acetyl]amino]-4-pentynoic acid;

ethyl 3S-[[2-[[[3-(aminocarbonylamino)phenyl]-carbonyl]amino]acetyl]amino]-4-pentynoate;

β S-[[2-[[[3-[(aminoiminomethyl)amino]-2,5,6-trifluorophenyl]carbonyl]amino]acetyl]-amino]-4-pentynoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

ethyl (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-[1,1'-biphenyl]-4-propanoic acid;

- 740 -

ethyl (\pm) β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-[1,1'-biphenyl]-4-propanoate;

(\pm) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-naphthalene-1-carboxylic acid;

methyl (\pm) β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-naphthalene-1-carboxylate;

(\pm) 3-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]-2-oxopyrrolidine-1-propanoic acid;

3R-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-4-pentynoic acid;

ethyl 3R-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-4-pentynoate;

3S-[[2-[[[3-[[[(phenylmethyl)amino]-carbonyl]amino]phenyl]carbonyl]amino]acetyl]-amino]-4-pentynoic acid;

ethyl 3S-[[2-[[[3-[[[(phenylmethyl)amino]-carbonyl]amino]phenyl]carbonyl]amino]acetyl]-amino]-4-pentynoate;

- 741 -

3S-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-pentynoic acid;

β -[[2-[[[3-(aminocarbonylamino)phenyl]-
carbonyl]amino]acetyl]amino]pyridine-
3-propanoic acid;

ethyl β -[[2-[[[3-(aminocarbonylamino)phenyl]-
carbonyl]amino]acetyl]amino]pyridine-3-propanoate;

(\pm) β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

(\pm) ethyl β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoate;

(\pm) ethyl β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]-
amino]furan-2-propanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
furan-3-propanoic acid;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]-
amino]acetyl]amino]pentanedioic acid;

bismethyl ester 3-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]-amino]acetyl]amino]pentanedioate;

(\pm) hydrogen methyl 3-[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pentanedioate;

- 742 -

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-furan-2-propanoic acid;

ethyl (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]furan-2-propanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-naphthalene-2-propanoic acid;

(±) methyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-thiophene-3-propanoate;

ethyl 3S-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-pentynoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-thiophene-3-propanoic acid;

(±) 2-[3-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-carboxybutyl]thio]benzoic acid;

(±) 2-[3-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-carboxybutyl]sulfonyl]benzoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-thiophene-2-propanoic acid;

- 743 -

(±) methyl 2-[[3-[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-carboxybutyl]thio]benzoate;

(±) methyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-5-[(4-methylphenyl)thio]pentanoate;

(±) methyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4-[[[(4-methylphenyl)sulfonyl]amino]butanoate];

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4-[[[(4-methylphenyl)sulfonyl]amino]butanoic acid];

(±) 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-5-[(4-methylphenyl)thio]pentanoic acid;

(±) 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-5-[(4-methylphenyl)sulfonyl]pentanoic acid;

3S-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4-(phenylthio)butanoic acid;

3R-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4-pentynoic acid;

ethyl 3R-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4-pentynoate;

- 744 -

2-[[2S-[[2-[[[3-(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-2-
(carboxymethyl)ethyl]sulfonyl]benzoic acid;

3S-[[2-[[[3-(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
4-pentynoic acid;

ethyl 3S-[[2-[[[3-(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
4-pentynoate;

2-[[2S-[[2-[[[3-(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-2-
(carboxymethyl)ethyl]thio]benzoic acid;

(±)ethyl β-[[2-[[[3-(aminoiminomethyl)-
amino]phenyl]carbonyl]methylamino]acetyl]-
amino]pyridine-3-propanoate;

(±)β-[[2-[[[3-(aminoiminomethyl)amino]phenyl]-
carbonyl]methylamino]acetyl]amino]pyridine-
3-propanoic acid;

(±)ethyl β-[[2-[[[3-(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]-1-oxopropyl]-
amino]pyridine-3-propanoate;

(±)β-[[2-[[[3-(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]-1-oxopropyl]-
amino]pyridine-3-propanoic acid;

(±) β-[[2-[[[3-(aminoiminomethyl)amino]-4-
methylphenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

- 745 -

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-methyl]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoic acid;

3S-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-hydroxybutanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]-amino]-2-hydroxybenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-2-hydroxy-5-methylbenzenepropanoic acid;

(±) 3-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-[(2-hydroxyethyl)amino]-4-oxobutanoic acid;

2S-[[2-[[[3-[[aminoiminomethyl]amino]phenyl]-carbonyl]amino]acetyl]amino]-3-carboxypropyl 2-aminobenzoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-1,4-benzodioxin-6-propanoic acid;

N-[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]- β -alanine, ethyl ester;

N-[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]- β -alanine;

- 746 -

(±)ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-quinoline-3-propanoate;

β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-quinoline-3-propanoic acid;

N-[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]-β-alanine, ethyl ester;

3-[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]amino]propanoic acid;

(±)ethyl β-[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoate;

(±) β-[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoic acid;

ethyl β-[[2-[[[3-[[[(phenylamino)carbonyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate;

- 747 -

β -[[2-[[[3-[(phenylamino)carbonyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-(aminocarbonylamino)-phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate;

β -[[2-[[[3-(aminocarbonylamino)phenyl]-carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(4-methylphenyl)sulfonyl]-amino]carbonyl]amino]phenyl]carbonyl]amino]-acetyl]amino]pyridine-3-propanoate;

β -[[2-[[[3-[[[(4-methylphenyl)sulfonyl]amino]-carbonyl]amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(aminothioxomethyl)-amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

β -[[2-[[[3-[(aminothioxomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(aminothioxomethyl)amino]-phenyl]carbonyl]amino]acetyl]-amino]benzenepropanoate;

β -[[2-[[[3-[(aminothioxomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

- 748 -

ethyl β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoate;

β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoic acid;

ethyl β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]-1,3-benzodioxole-5-propanoate;

β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
1,3-benzodioxole-5-propanoic acid;

ethyl β -[[2-[[[3-3-[[[(phenylamino)carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
1,3-benzodioxole-5-propanoate;

β -[[2-[[[3-3-[[[(phenylamino)carbonyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-1,3-
benzodioxole-5-propanoic acid;

β -[[2-[[[3-[[[(4-(aminosulfonyl)phenylmethyl)-
amino]carbonyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]pyridine-
3-propanoic acid;

β -[[2-[[[3-[[[(3-pyridinylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

β -[[2-[[[3-[[[(2-carboxyethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

- 749 -

β -[[2-[[[3-[[[(2-phenylethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

β -[[2-[[[3-[[[(1-naphthalenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-4-
chlorophenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-4-
chlorophenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoic acid;

β -[[2-[[[5-[(aminoiminomethyl)amino]-2-chlorophenyl]-
carbonyl]amino]acetyl]amino]benzenepropanoic acid;

ethyl β -[2-[[[3-[[amino(aminocarbonyl)-
imino]methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]-3,5-
dichlorobenzenepropanoate;

β -[[2-[[[3-[[amino(aminocarbonyl)imino]-
methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]-3,5-dichlorobenzene-
propanoic acid;

[(dimethylamino)carbonyl]methyl β -
[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-
dichlorobenzenepropanoate;

1,1-dimethylethyl 3,5-dichloro- β -[[2-[[[3[[[(ethoxy-
carbonyl)amino][(ethoxycarbonyl)imino]methyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

- 750 -

3,5-dichloro- β -[[2-[[[3-[[[(ethoxycarbonyl)-
amino]([thoxycarbonyl)imino]methyl]-
amin]-phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-4-
chlorophenyl]carbonyl]amino]acetyl]amino]-
3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-4-
chlorophenyl]carbonyl]amino]acetyl]amino]-
3,5-dichlorobenzenepropanoic acid;

ethyl 3S-[[2-[[[3-[[amino[(aminocarbonyl)imino]-
methyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]-4-pentynoate;

3S-[[2-[[[3-[[amino[(aminocarbonyl)imino]-
methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]-4-pentynoic acid;

ethyl 3S-[[2-[[[3-[(aminoiminomethyl)-
amino]-4-chlorophenyl]carbonyl]amino]-
acetyl]amino]-4-pentynoate;

3S-[[2-[[[3-[(aminoiminomethyl)amino]-4-
chlorophenyl]carbonyl]amino]acetyl]-
amino]-4-pentynoic acid;

(\pm) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-3,4-
dichlorobenzenepropanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,4-
dichlorobenzenepropanoic acid;

- 751 -

(±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)carbonyl]amino]acetyl]amino]-3,4-dichlorobenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-2,5-dimethylbenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-2,5-dimethylbenzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-chlorobenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-chlorobenzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-bromobenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-bromobenzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-bromobenzenepropanoate;

- 752 -

- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-bromobenzenepropanoic acid;
- (±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethylbenzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethylbenzenepropanoic acid;
- (±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethoxybenzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethoxybenzenepropanoic acid;
- (±) (2,2-dimethyl-1-oxopropoxy)methyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;
- (±) β -[[2-[[[3-[[[(aminocarbonyl)imino)-methylamino)methyl]amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminothioxomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,4-dibromobenzenepropanoic acid;

- 753 -

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-fluoro-5-(trifluoromethyl)benzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-fluorobenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromobenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-methylbenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromobenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-chlorobenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-chlorobenzenepropanoic acid;

(±) [2-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]ethyl] β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-iodobenzenepropanoic acid;

- 754 -

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2-hydroxy-4-methoxybenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-5-hydroxy-4-methoxybenzofuran-6-propanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-9H-fluorene-2-propanoic acid;

ethyl(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-9H-fluorene-2-propanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-dichloro-2-hydroxybenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2-hydroxy-5-nitrobenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromo-2-hydroxybenzenepropanoic acid;

ethyl(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromo-2-hydroxybenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromo-2-hydroxybenzenepropanoic acid;

- 755 -

ethyl(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-5-bromo-2-hydroxybenzenepropanoate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-cyclohexanepropanoic acid;

ethyl(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-cyclohexanepropanoate;

ethyl(±) β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichloro-2-hydroxybenzenepropanoate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-5-chloro-2-hydroxybenzenepropanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-chloro-2-hydroxybenzenepropanoic acid;

(±) 5-amino-β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-2-hydroxybenzenepropanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromopyridine-3-propanoic acid;

ethyl(±) β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromopyridine-3-propanoate;

- 756 -

3,5-dichloro- β -[[2-[[[3-[[[(ethoxycarbonyl)amino]-thioxomethyl]amino]phenyl]carbonyl]amino]-acetyl]amino]benzenepropanoic acid;

3,5-dichloro- β -[[2-[[[3-[[[(ethoxycarbonyl)amino]-iminomethyl]amino]phenyl]carbonyl]amino]-acetyl]amino]benzenepropanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino][1,1'-biphenyl]-3-propanoic acid;

1,1-dimethylethyl β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino][1,1'-biphenyl]-3-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]-amino]acetyl]amino][pyrimidine-5-propanoic acid;

1,1-dimethylethyl β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-[pyrimidine-5-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]-amino]acetyl]amino]-3-methylthiophene-2-propanoic acid;

1,1-dimethylethyl β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3-methylthiophene-2-propanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3-(methylthio)-benzenepropanoic acid;

- 757 -

1,1-dimethylethyl (\pm) β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3-(methylthio)benzenepropanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-6-methylpyridine-2-propanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-(methylsulfonyl)-benzenepropanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-diethoxybenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-diethoxybenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4-bromothiophene-2-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4-bromothiophene-2-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-5-chlorothiophene-2-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-5-chlorothiophene-2-propanoate;

- 758 -

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-1H-pyrazole-
3-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-1H-pyrazole-
3-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-5-methylthiophene-
2-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-5-methylthiophene-
2-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-2,3,5-trichloro-
benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-2,3,5-trichloro-
benzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-2(carboxymethoxy)-
benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-2(carboxymethoxy)-
benzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-4-methoxy-1,3-
benzodioxole-6-propanoic acid;

- 759 -

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-methoxy-1,3-
benzodioxole-6-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-5-bromo-
2-methoxybenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-5-bromo-
2-methoxybenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-6-chloro-
1,3-benzodioxole-5-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-6-chloro-
1,3-benzodioxole-5-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzofuran-2-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzofuran-2-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-3-
(carboxymethoxy)benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-3-
(carboxymethoxy)benzenepropanoate;

- 760 -

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4,4,4-
trifluorobutanoic acid;

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4,4,4-
trifluorobutanoate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3-bromo-4,5-
dimethoxybenzenepropanoic acid;

ethyl(±) β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3-bromo-4,5-
dimethoxybenzenepropanoate;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-
methylpentanoic acid;

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-
methylpentanoate;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
phenyl]carbonyl]amino]acetyl]amino]-
pentanoic acid;

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
phenyl]carbonyl]amino]acetyl]amino]-
pentanoate;

β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
5-bromo-3-chloro-2-hydroxybenzene-
propanoic acid;

- 761 -

β -[[2-[[[3-[[[(4-pyridinylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(4-pyridinylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]pyridine-3-propanoate;

3,5-dichloro- β -[[2-[[[3-[[[(4-pyridinylmethyl)-
amino]carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoic acid;

ethyl 3,5-dichloro- β -[[2-[[[3-[[[(4-pyridinylmethyl)-
amino]carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[[[(2-pyridinylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(2-pyridinylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate;

3,5-dichloro- β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoic acid;

ethyl 3,5-dichloro- β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

3-chloro- β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoic acid;

- 762 -

ethyl 3-chloro- β -[[2-[[[3-[[[(phenylmethyl)-
amino]carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[[[(1-phenylethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(1-phenylethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoate;

β -[[2-[[[3-[[[(1H-benzimidazol-2-yl)-methyl]amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-[[[(1H-benzimidazol-2-yl)-methyl]-
amino]carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]-
amino]carbonyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]pyridine-3-
propanoic acid;

ethyl β -[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]-
amino]carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]pyridine-3-propanoate;

3-[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]-
amino]carbonyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]butanoic acid;

ethyl 3-[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]-
amino]carbonyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]butanoate;

- 763 -

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-bis(1-methyl-
ethoxy)benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-bis(1-methyl-
ethoxy)benzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dibromo-4-
hydroxybenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dibromo-4-
hydroxybenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dichloro-4-
hydroxybenzenepropanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dichloro-4-
hydroxybenzenepropanoate;

β -[[2-[[[5-[(aminoiminomethyl)amino]-2-
hydroxyphenyl]carbonyl]amino]acetyl]amino]-
3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[5-[(aminoiminomethyl)amino]-2-
hydroxyphenyl]carbonyl]amino]acetyl]amino]-
3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[(phenoxyamino)carbonyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

- 764 -

ethyl β -[[2-[[[3-[(phenoxyamino)carbonyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate;

β -[[2-[[[3-[(phenylamino)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(phenylamino)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-5-[(3,5-dichlorophenyl)amino]-5-oxopentanoic acid;

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-5-[(3,5-dichlorophenyl)amino]-5-oxopentanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxy-phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxy-phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxy-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxy-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

- 765 -

β -[[2-[[[3,5-bis[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dichloro-
benzenepropanoic acid;

ethyl β -[[2-[[[3,5-bis[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-3,5-dichloro-
benzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-5-
(trifluoroacetyl)amino]phenyl]carbonyl]amino]acetyl]-
amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-
(trifluoroacetyl)amino]phenyl]carbonyl]amino]acetyl]-
amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-(acetylamino)-5-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-(acetylamino)-5-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
3,5-dichlorobenzenepropanoate;

(\pm) 3,5-dichloro- β -[[2-[[[3-
[[[(methylamino) (methyylimino)methyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoic acid;

(\pm) 3,5-dichloro- β -[[2-[[[3-
[[[(ethylamino) (methyylimino)methyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoic acid;

- 766 -

(±) 3,5-dichloro-β-[[2-[[[3-[[[(1-methylethyl)amino](methylimino)methyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

(±) β-[[2-[[[3-[[[(ethylamino)-(methylimino)methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]-4-fluorobenzene-propanoic acid;

(±) 4-fluoro-β-[[2-[[[3-[[[(4-pyridinylmethyl)amino](methylimino)methyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-4-fluorobenzenepropanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-1H-imidazole-2-propanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2,3,4,6-tetrafluorobenzenepropanoic acid;

β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromothiophene-2-propanoic acid;

β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-2-mercaptobenzenepropanoic acid;

and

- 767 -

(±) β -[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-5-chloro-2-mercaptobenzenepropanoic acid.

5. A compound according to Claim 3 wherein Y^1 is $N-R^2$ and R^2 is cyano.

6. A compound according to Claim 5 wherein the compound is selected from the group consisting of

phenylmethyl β -[[2-[[[3-[(cyanoimino)-phenylmethylamino)methyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

phenylmethyl β -[[2-[[[3-[(cyanoimino)-methylamino)methyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

phenylmethyl β -[[2-[[[3-[(cyanoimino)-(amino)methyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[(cyanoimino)(ethylamino)methyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[(cyanoimino)[(phenylmethyl)-amino]methyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

β -[[2-[[[3-[(cyanoimino)(methylamino)-methyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

β -[[2-[[[3-[[amino(cyanoimino)methyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

- 768 -

β -[[2-[[[3-[(cyanoimino)(ethylamino)-
methyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoic acid;

ethyl 3S-[[2-[[[3-[(cyanoimino)-
(methylamino)methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]-4-pentynoate;

3S-[[2-[[[3-[(cyanoimino)(methylamino)-
methyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]-4-pentynoic acid;

ethyl β -[[2-[[[3-[(cyanoimino)[2-pyridinylmethyl]-
amino]methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[(cyanoimino)[2-pyridinylmethyl]-
amino]methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoic acid;

ethyl β -[[2-[[[3-[(cyanoimino)[3-
pyridinylmethyl]amino]methyl]amino]phenyl]-
carbonyl]amino]acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[(cyanoimino)[3-pyridinylmethyl]-
amino]methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoic acid;

ethyl 3S-[[2-[[[3-[[[(4-(aminosulfonyl)-
phenylmethyl]amino)(cyanoimino)methyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]-4-pentynoate;

3S-[[2-[[[3-[[[(4-(aminosulfonyl)phenylmethyl)-
amino](cyanoimino)methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]-4-pentynoic acid;

- 769 -

ethyl β -[[2-[[[3-[[amino(cyanoimino)methyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[[amino(cyanoimino)methyl]amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

(\pm) ethyl 3,5-dichloro- β -[[2-[[[3-[(cyanoimino)-(methylamino)methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoate;

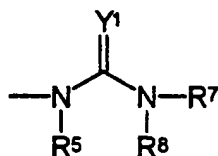
(\pm) 3,5-dichloro- β -[[2-[[[3-[(cyanoimino)(methylamino)methyl]amino]phenyl]carbonyl]amino]acetyl]-amino]benzenepropanoic acid;

and

ethyl 3-[[2-[[[3-[[amino(cyanoimino)methyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-4-pentynoate.

7. A compound according to Claim 2 wherein

A is



wherein Y^1 is N-R^2 ; R^2 taken together with R^7 forms a 4-12 membered ring; and R^5 and R^8 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, bicycloalkyl substituted alkyl, arylalkyl, aryloxy, hydroxy, alkoxy, amino, alkylamino, arylamino, amido, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkylcarbonyl, haloalkoxycarbonyl,

- 770 -

alkylthiocarbonyl, arylthiocarbonyl, acyloxymethoxycarbonyl, substituted phenyl, arylacyl, monocyclic and bicyclic heterocycles, monocyclic and bicyclic heterocyclicalkyl and -SO₂R¹⁰ wherein R¹⁰ is selected from the group consisting of alkyl, amino and aryl which are all optionally substituted with one or more substituent selected from the group consisting of acylamino, amino, carbonyl cyano, nitro, alkoxy, halo, alkyl, trifluoroalkyl, amido, alkylaminosulfonyl, alkylsulfonyl, alkylsulfonylamino, alkylamino, dialkylamino, aryloxy, thio, trifluoromethylthio, trifluoroalkoxy, and trifluoromethylsulfonyl or -NR⁷ and R⁸ taken together form a 4-12 membered ring wherein said ring optionally contains a heteroatom selected from the group consisting of O, N, and S wherein said ring is optionally substituted.

8. A compound according to Claim 7 wherein

V is -N(R⁶)- wherein R⁶ is selected from the group consisting of H and lower alkyl;

n is 1;

t is 0; and

p is 1.

- 771 -

9. A compound according to Claim 8 selected from the group consisting of

(±) ethyl β -[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

(±) β -[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

(±) ethyl β -[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoate;

(±) β -[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]-3,5-dichlorobenzenepropanoate;

(±) β -[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

(±) ethyl 3,5-dichloro- β -[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoate;

(±) 3,5-dichloro- β -[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]-carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

- 772 -

(±) 3,5-dibromo-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoic acid;

(±) 3-bromo-5-chloro-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]-carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

(±) [2-[2-[2-(2-hydroxyethoxy)-ethoxy]ethoxy]ethyl] 3,5-dichloro-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]-carbonyl]amino]acetyl]amino]benzenepropanoate;

(±) [2-[2-(2-hydroxyethoxy)-ethoxy]ethoxy]ethyl 3,5-dichloro-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoate;

(±) 3-bromo-5-chloro-2-hydroxy-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

ethyl (±) 3-bromo-5-chloro-2-hydroxy-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoate;

(±) 3,5-dichloro-2-hydroxy-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

- 773 -

(±) 3,5-dichloro- β -[[2-[[[3-[(4,5-dihydro-1H-pyrrolidin-2-yl)amino]phenyl]carbonyl]amino]-amino]acetyl]amino]-2-hydroxybenzenepropanoic acid;

(±) 3-bromo-5-chloro- β -[[2-[[[3-[(4,5-dihydro-1H-pyrrolidin-2-yl)amino]phenyl]carbonyl]amino]-acetyl]amino]-2-hydroxybenzenepropanoic acid;

β -[[2-[[[3-[(5-phenyl-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(5-phenyl-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate;

(±) ethyl 3,5-dichloro- β -[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoate;

(±) 3,5-dichloro- β -[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoic acid;

ethyl (±) 3,5-dichloro-2-hydroxy- β -[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoate;

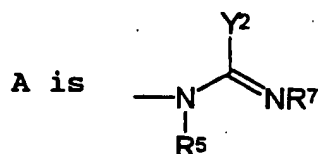
- 774 -

(±) 3-bromo-5-dichloro-2-hydroxy-
 β -[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-
dimethylpyrimidin-2-yl)amino]phenyl]-
carbonyl]amino]acetyl]amino]benzene-
propanoic acid;

and

ethyl(±) 3-bromo-5-dichloro-2-hydroxy- β -[[2-[[[3-
[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-
yl)amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoate.

10. A compound according to the formula of Claim 1
wherein



wherein Y^2 is selected from the group consisting of
lower alkyl, substituted alkyl, phenyl,
substituted phenyl, cycloalkyl, monocyclic
heterocycles, $-S-R^9$ and $-O-R^9$ wherein R^9 is selected
from the group consisting of H, alkyl, substituted
alkyl, phenyl, substituted phenyl and monocyclic
heterocycles or R^9 taken together with R^7 forms a
4-12 membered ring; or

Y^2 taken together with R^7 forms a 4-12 membered
ring which is optionally substituted.

- 775 -

11. A compound according to Claim 10 wherein

Y^2 taken together with R^7 forms a 4-12 membered ring which is optionally substituted.

12. A compound according to Claim 11 wherein

V is $-N(R^6)-$ wherein R^6 is selected from the group consisting of H and lower alkyl;

n is 1;

t is 0 or 1; and

p is 1.

13. A compound according to Claim 12 wherein the compound is selected from the group consisting of

(±) ethyl β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

(±) β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoic acid;

(±) ethyl β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-1,3-benzodioxole-5-propanoate;

(±) β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-1,3-benzodioxole-5-propanoic acid;

- 776 -

- (±) β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;
- (±) ethyl β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoate;
- β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid;
- (±) ethyl β -[[2-[[[4-chloro-3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoate;
- (±) β -[[2-[[[4-chloro-3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid;
- (±) β -[[2-[[[3,5-bis[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid;
- β S-[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-4-pentynoic acid;
- (±) ethyl β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;
- (±) β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

- 777 -

(±) ethyl β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]-3,5-dichlorobenzenepropanoate;

(±) β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

(±) ethyl 3,5-dichloro- β -[[2-[[[3-[(2,3,4,5-tetrahydropyridin-6-yl)amino]phenyl]-carbonyl]amino]acetyl]amino]benzenepropanoate;

(±) 3,5-dichloro- β -[[2-[[[3-[(2,3,4,5-tetrahydropyridin-6-yl)amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoic acid;

(±) 3,5-dichloro-2-hydroxy- β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

and

ethyl(±) 3,5-dichloro-2-hydroxy- β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoate.

14. A compound according to Claim 10 wherein

Y² is selected from the group consisting of lower alkyl, substituted alkyl, phenyl, substituted phenyl, cycloalkyl and monocyclic heterocycles.

- 778 -

15. A compound according to Claim 14 wherein

V is $-N(R^6)-$ wherein R^6 is selected from the group consisting of H and lower alkyl;

n is 1;

t is 0; and

p is 1.

16. A compound according to Claim 15 wherein the compound is selected from the group consisting of

(±) ethyl β -[[2-[[[3-[(iminophenylmethyl)-amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

β S-[[2-[[[3-[[imino(1-pyrrolidinyl)methyl]-amino]phenyl]carbonyl]amino]acetyl]-amino]-4-pentynoic acid;

(±) β -[[2-[[[3-[(iminophenylmethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

3,5-dichloro- β -[[2-[[[3-[[imino(1-piperidinyl)methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoic acid;

and

ethyl 3,5-dichloro- β -[[2-[[[3-[[imino(1-piperidinyl)methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoate.

- 779 -

17. A compound according to Claim 10 wherein Y^2 is $-S-R^9$ or $-O-R^9$ wherein R^9 is selected from the group consisting of H, alkyl, substituted alkyl, phenyl, substituted phenyl and monocyclic heterocycles or R^9 taken together with R^7 forms a 4-12 membered ring.

18. A compound according to Claim 17 wherein

V is $-N(R^6)-$ wherein R^6 is selected from the group consisting of H, lower alkyl, substituted alkyl, cycloalkyl, aryl, substituted aryl, monocyclic heterocycles and benzyl;

n is 0;

t is 0; and

p is 1 or 2.

19. A compound according to Claim 18 wherein the compound is selected from the group consisting of

ethyl β -[[2-[[[3-[(4,5-dihydrothiazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

β -[[2-[[[3-[(4,5-dihydrothiazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

β -[[2-[[[3-[(benzoxazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

thyl β -[[2-[[[3-[(benzoxazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate.

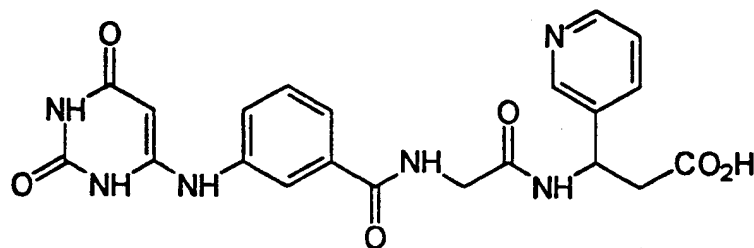
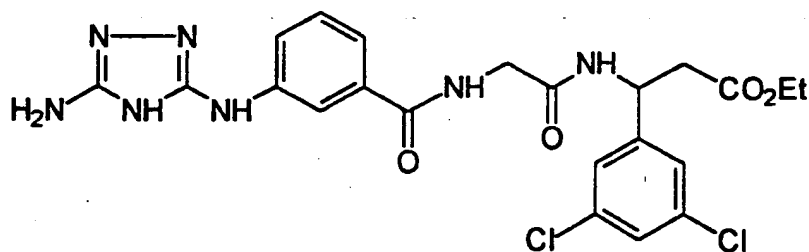
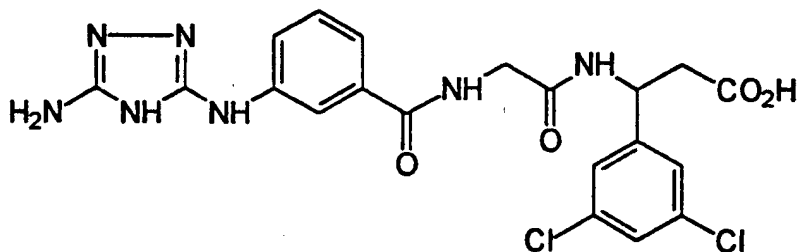
- 780 -

β -[[2-[[[3-[(5,6-dihydro-4H-thiazin-2-yl)-
amino]phenyl]carbonyl]amino]acetyl]amin]-
pyridine-3-propanoic acid;

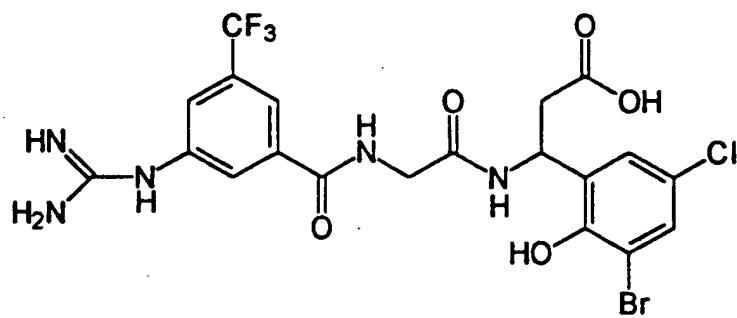
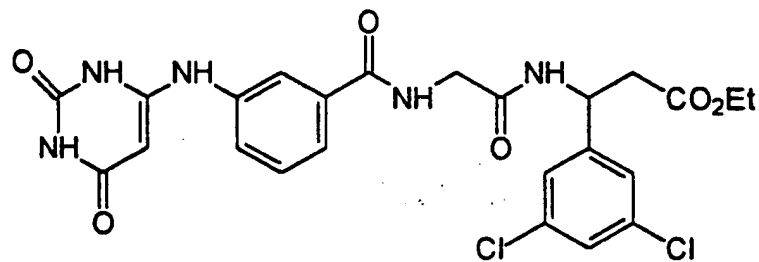
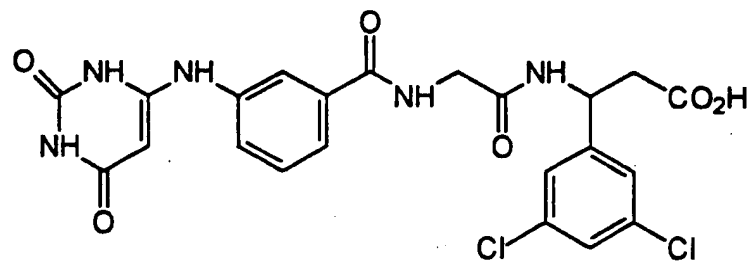
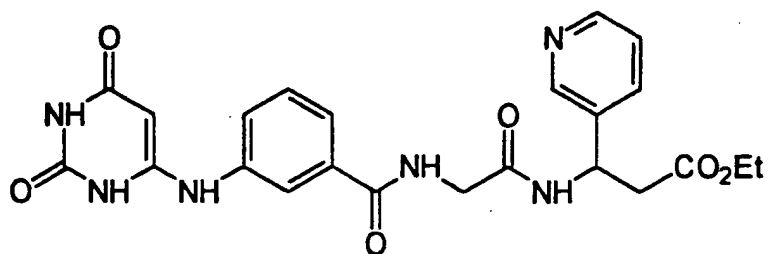
and

ethyl β -[[2-[[[3-[(5,6-dihydro-4H-thiazin-2-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate.

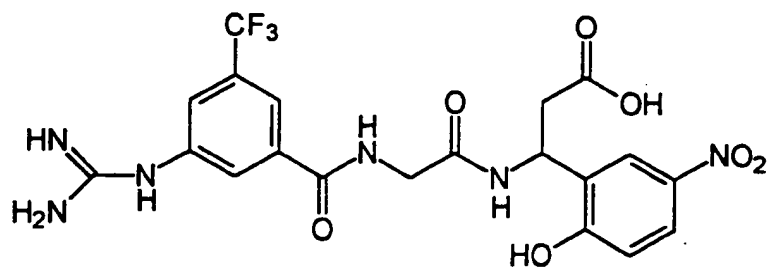
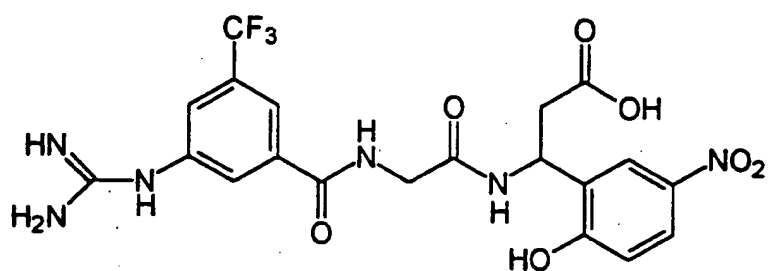
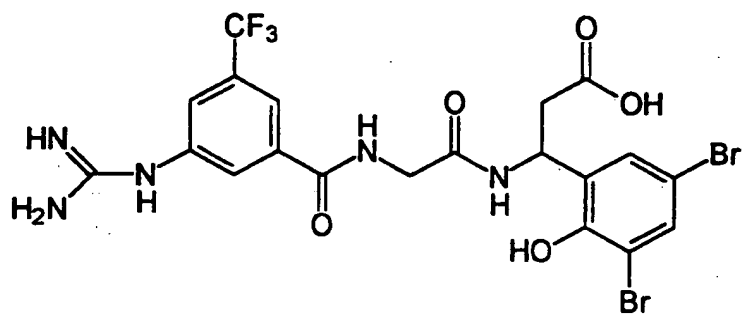
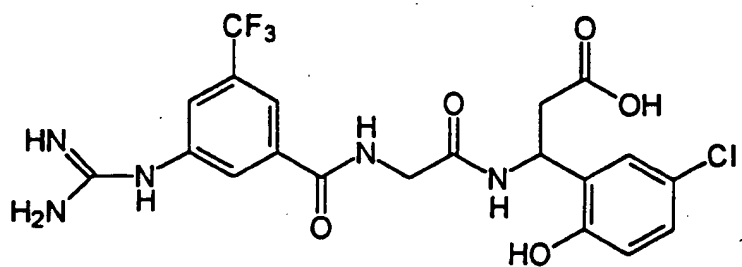
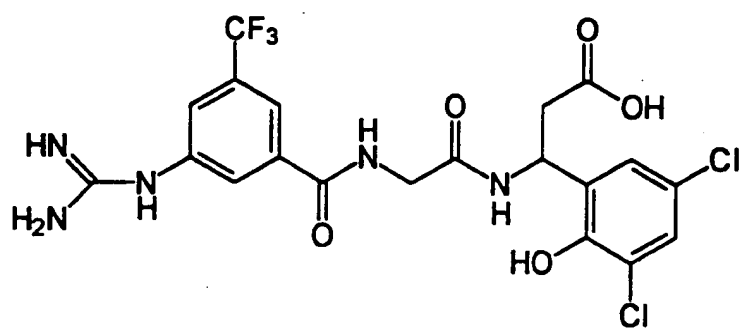
20. A compound according to Claim 1 of the formula



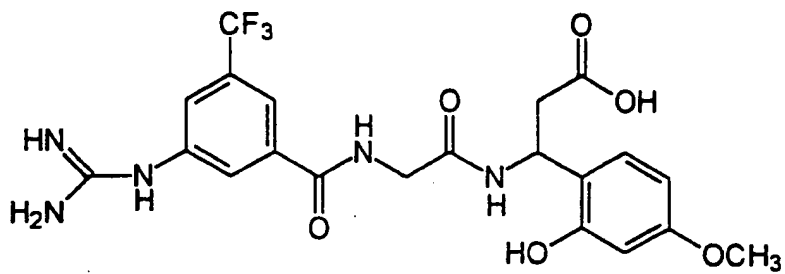
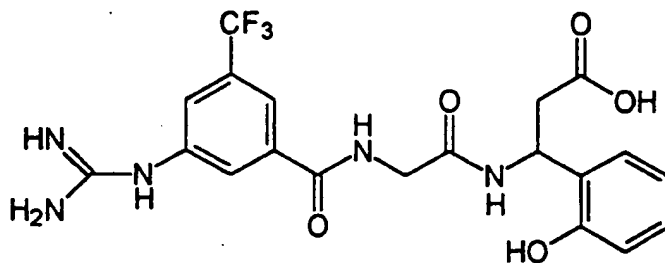
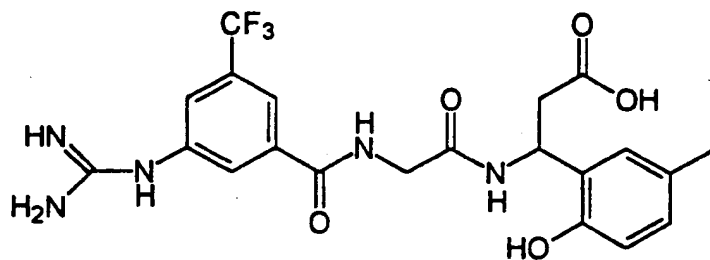
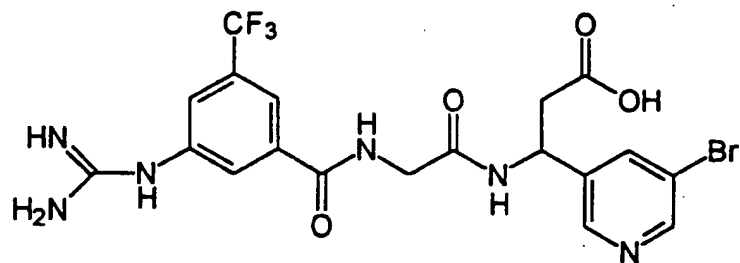
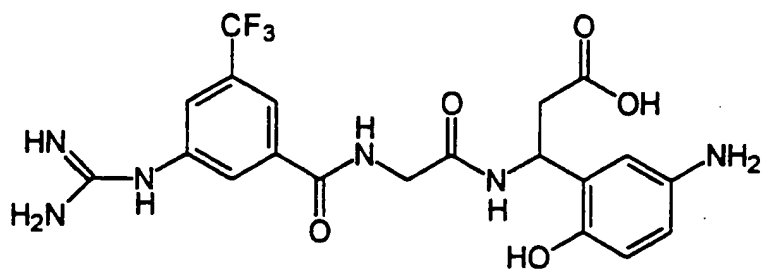
- 781 -



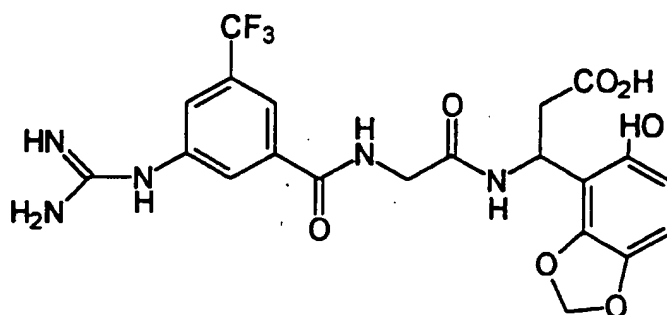
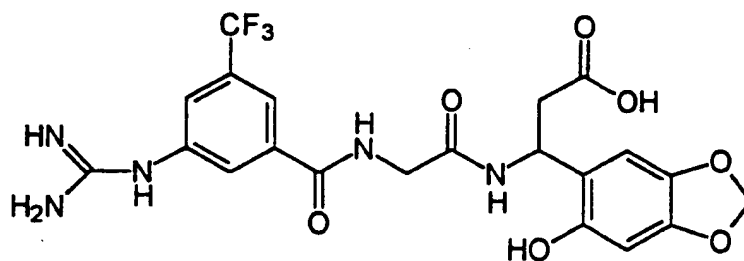
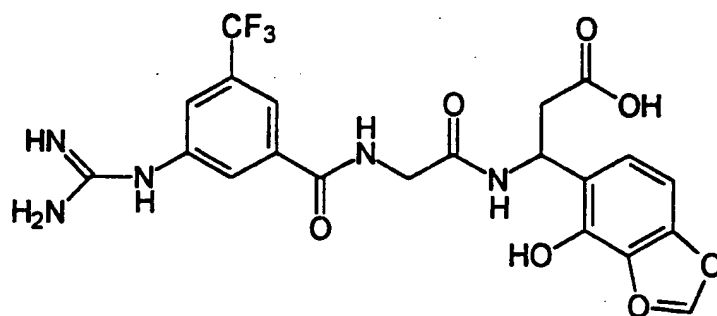
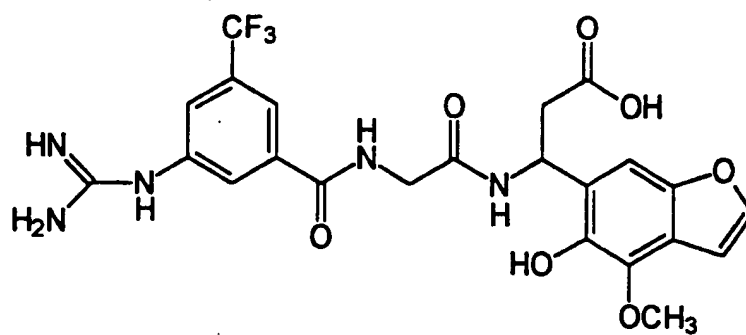
- 782 -



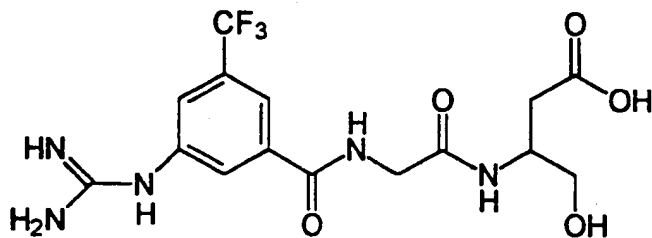
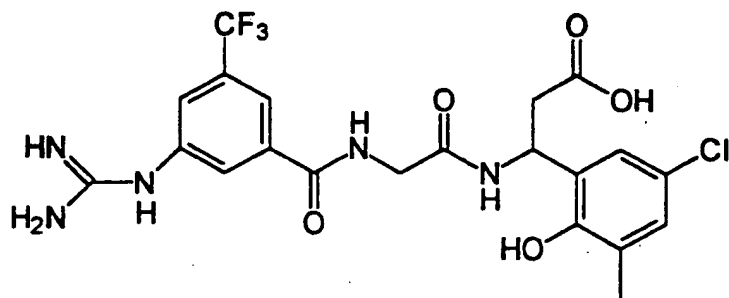
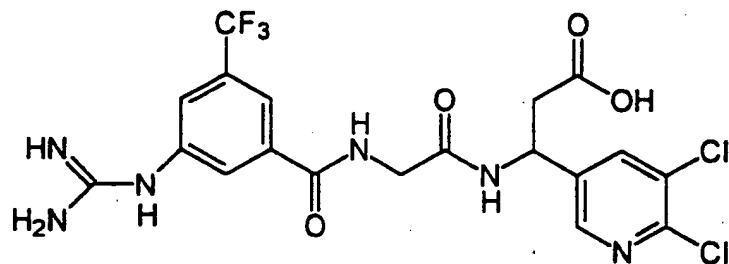
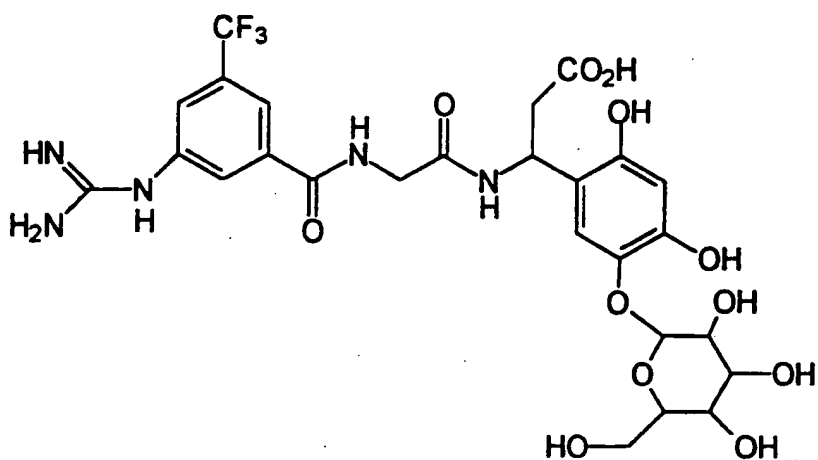
- 783 -



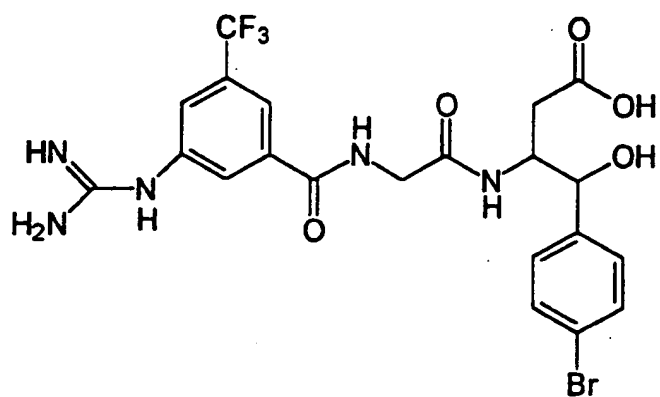
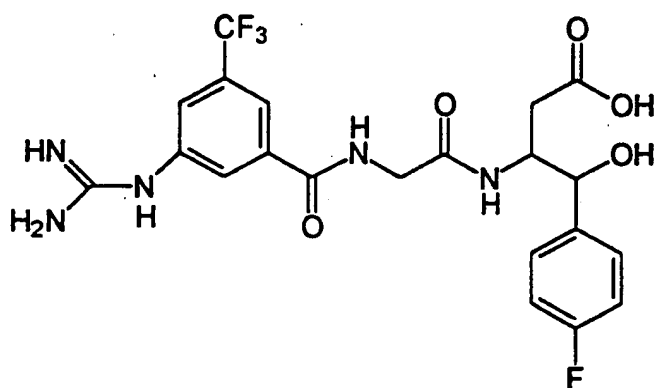
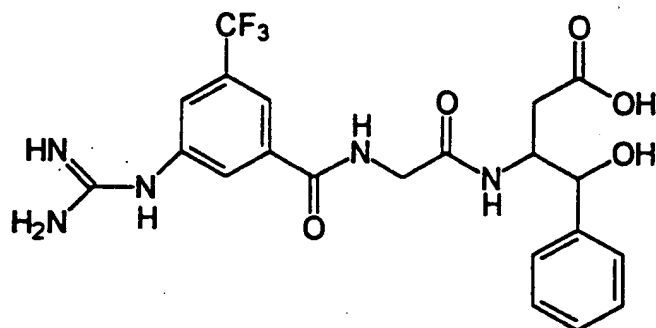
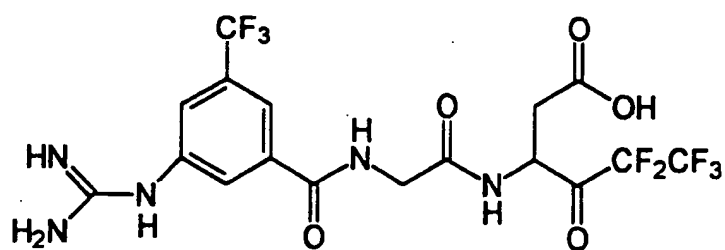
- 784 -



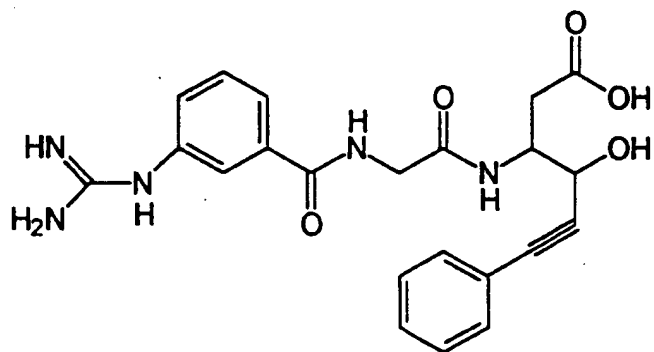
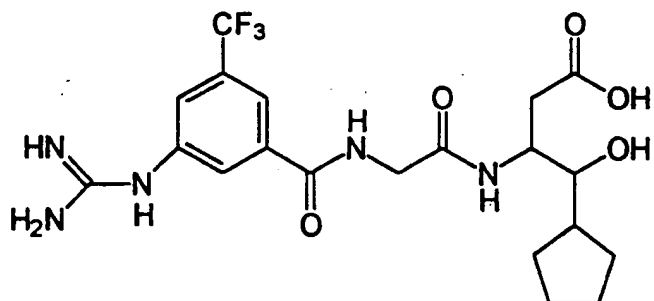
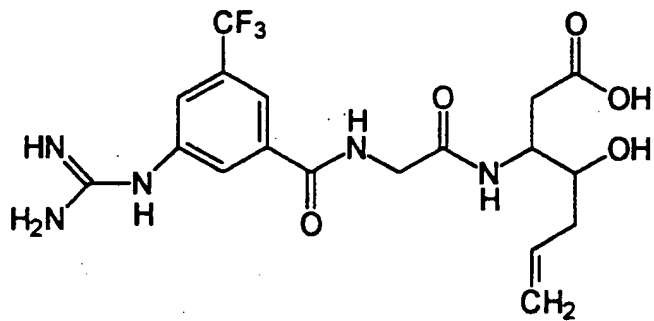
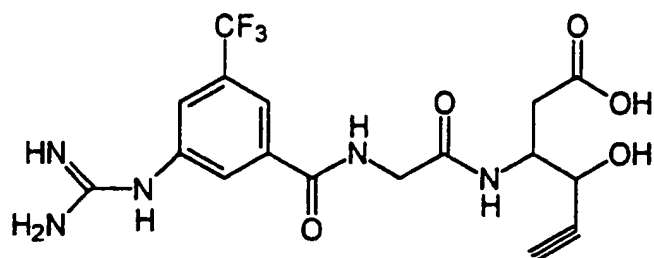
- 785 -



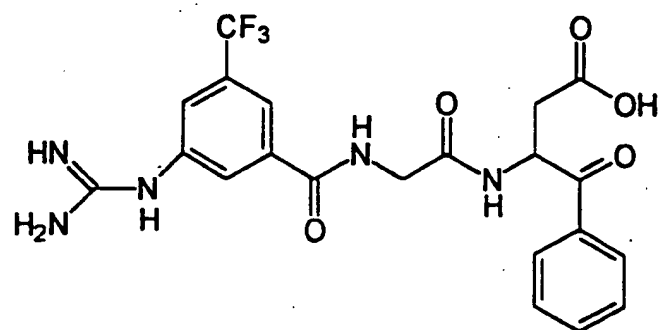
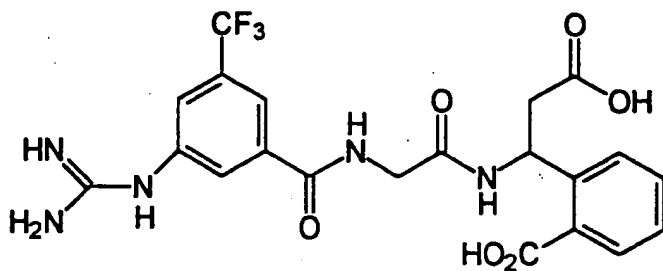
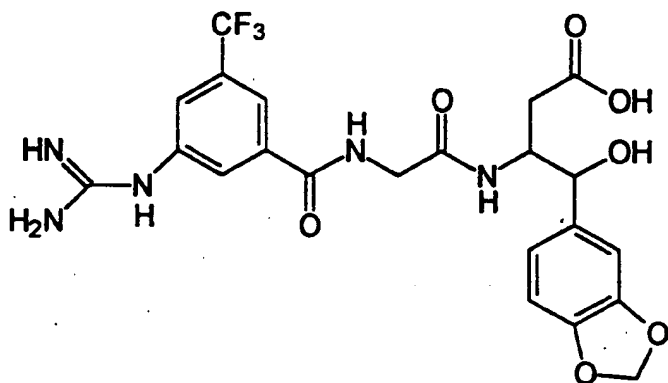
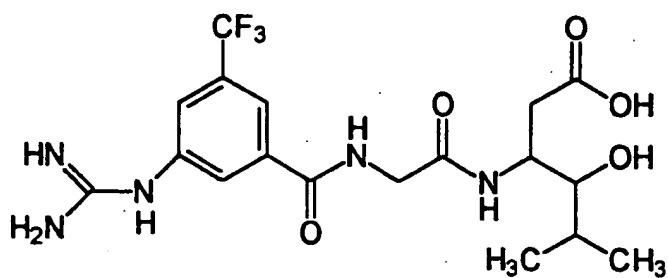
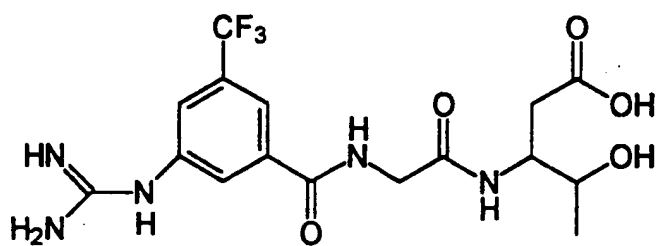
- 786 -



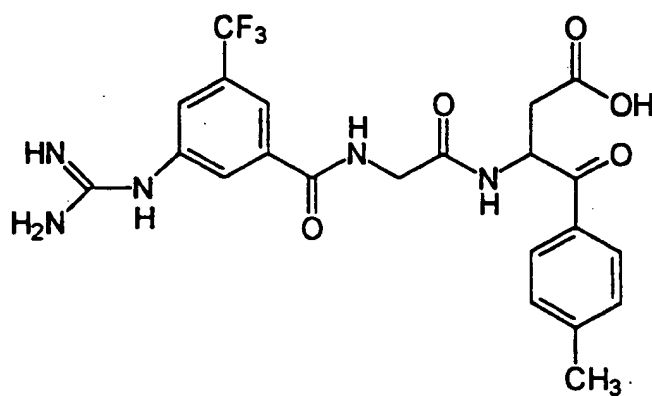
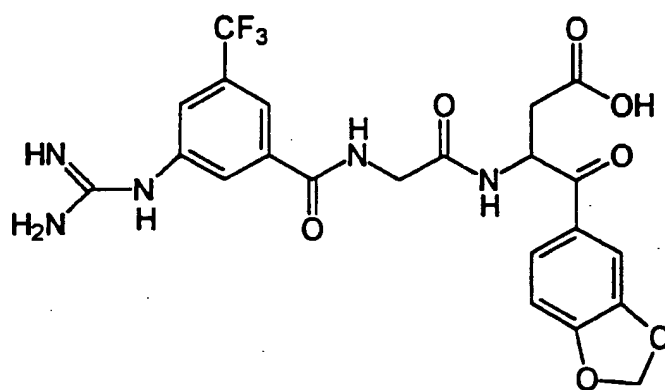
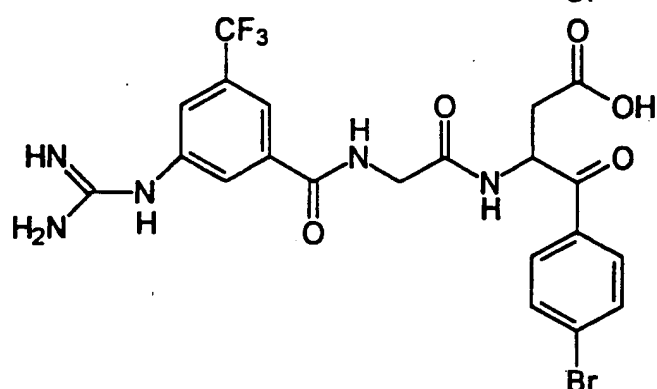
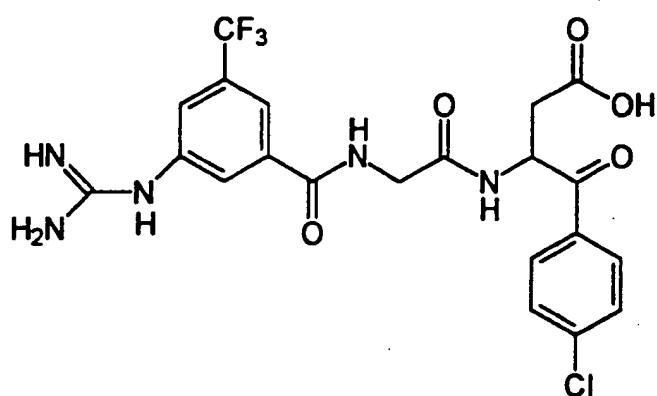
- 787 -



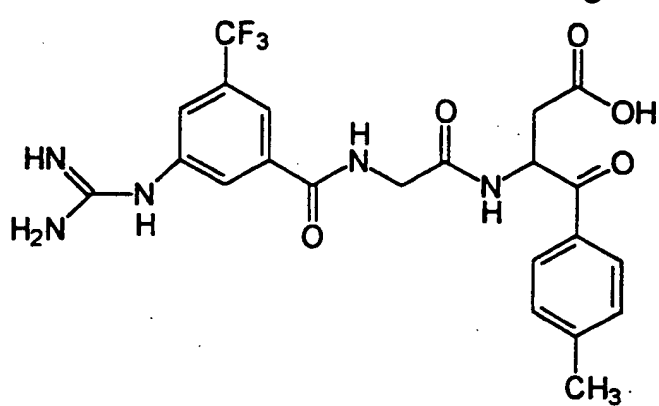
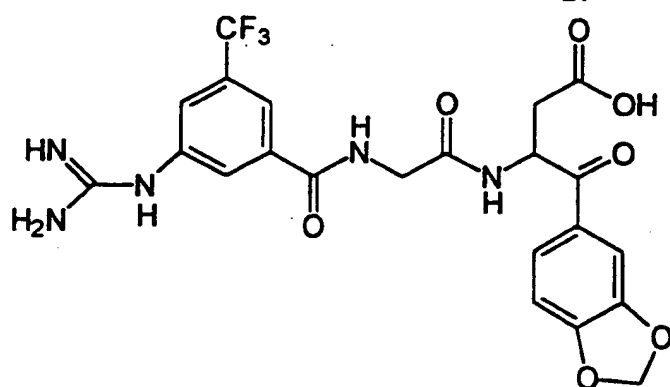
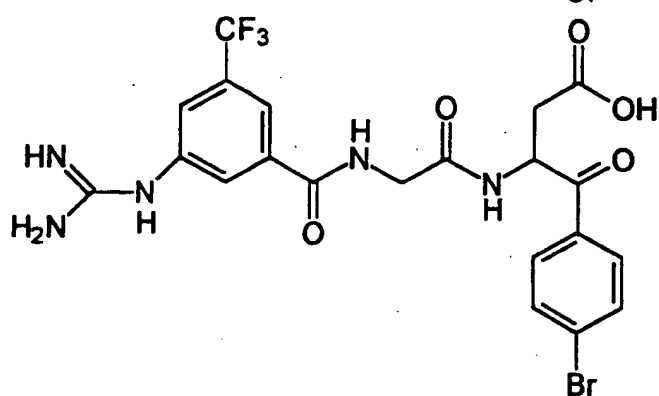
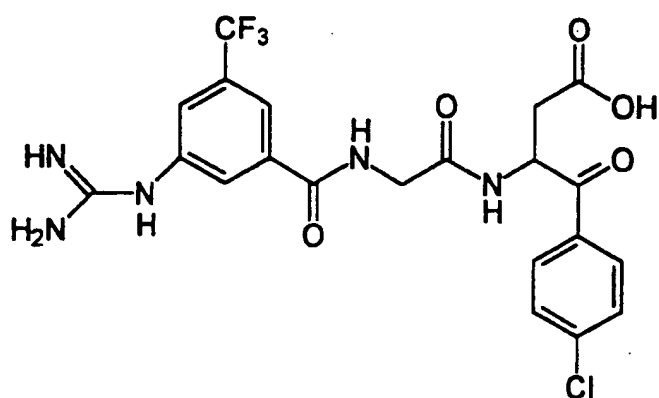
- 788 -



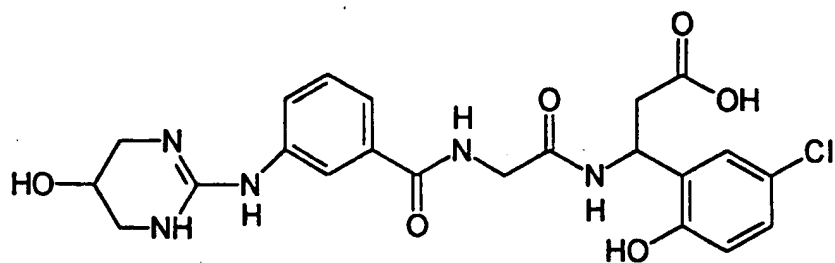
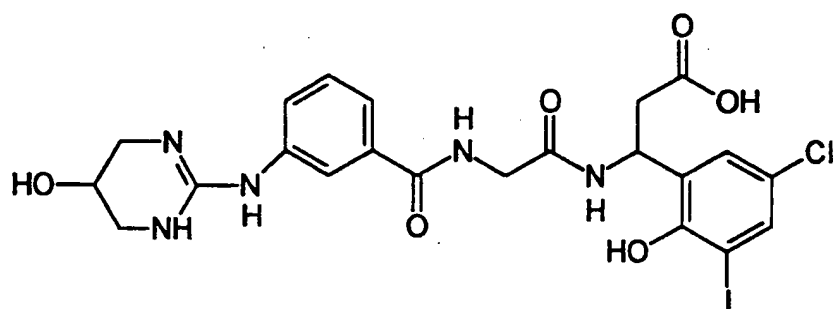
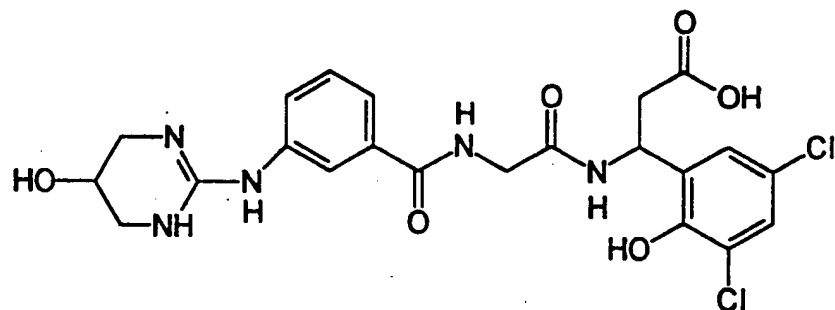
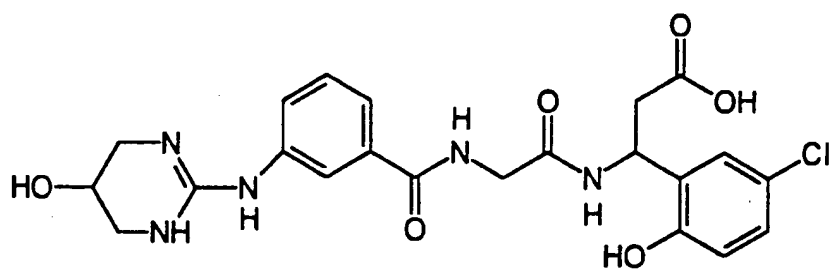
- 789 -



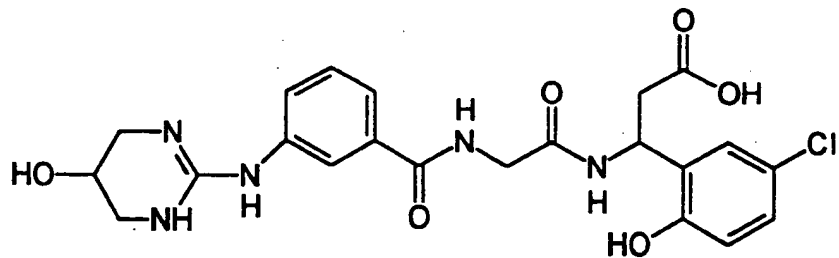
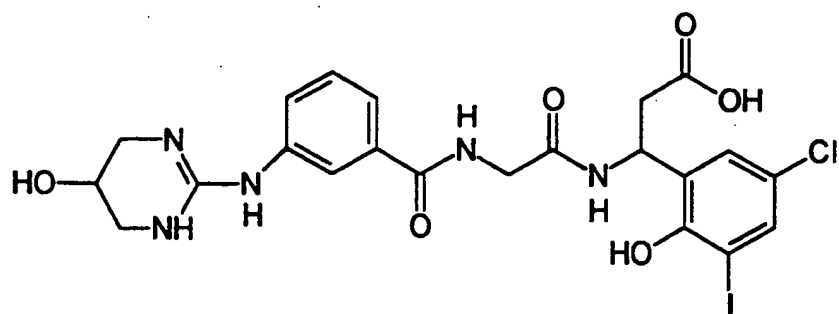
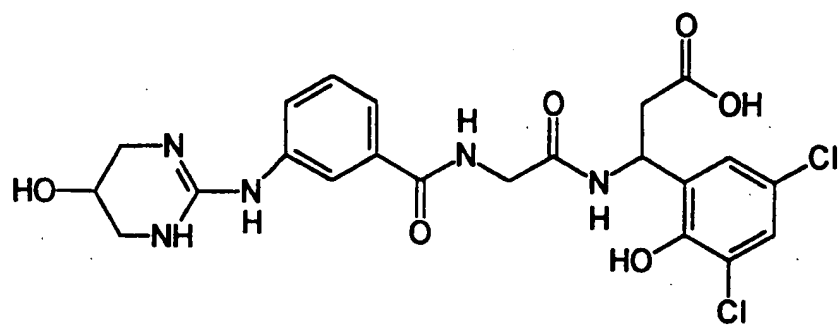
- 790 -



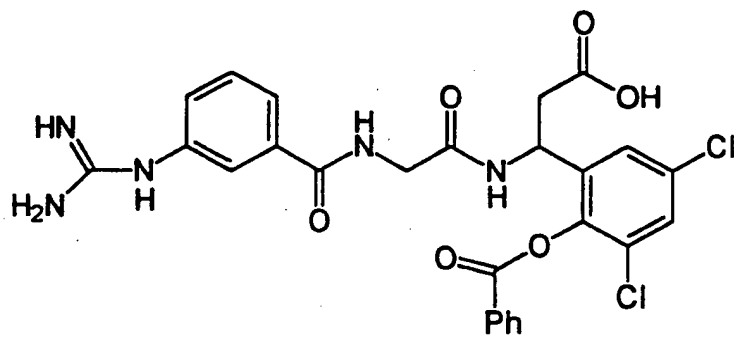
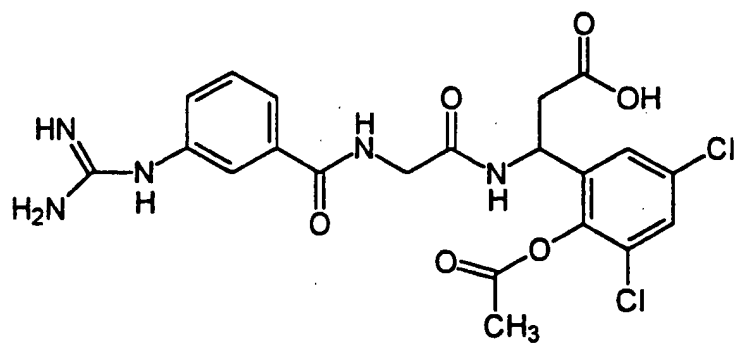
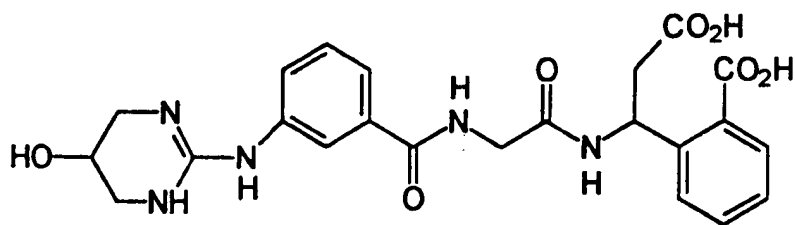
- 791 -



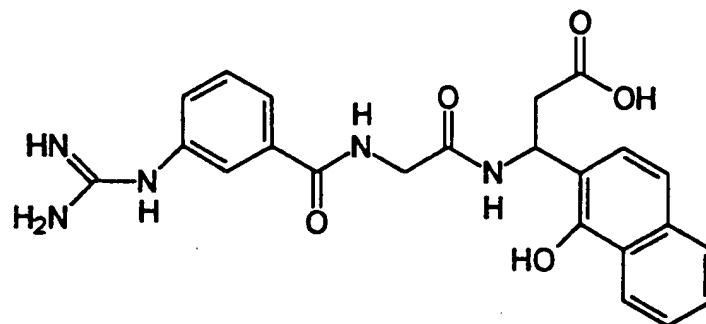
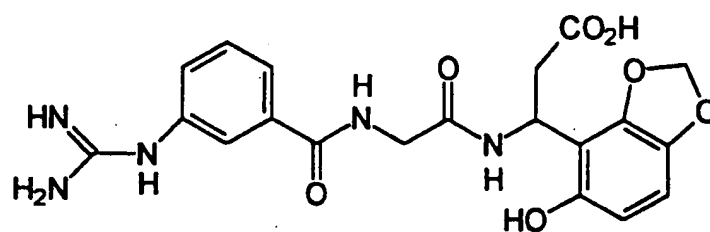
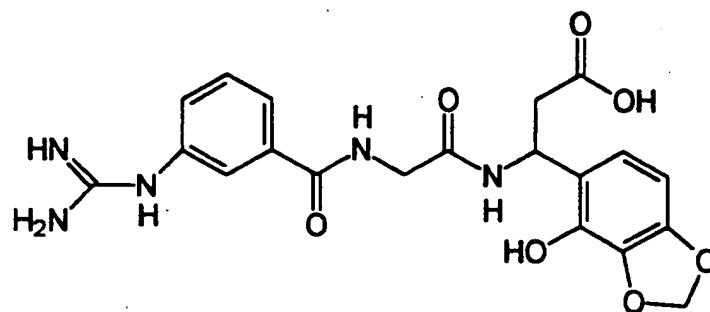
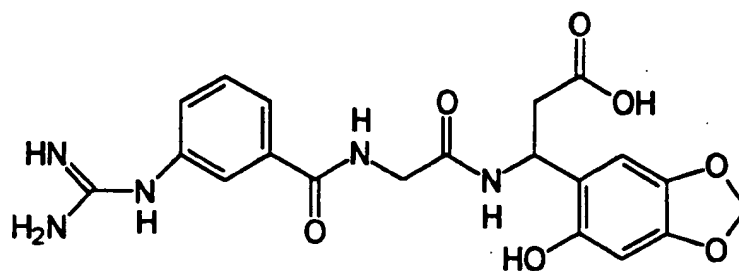
- 792 -



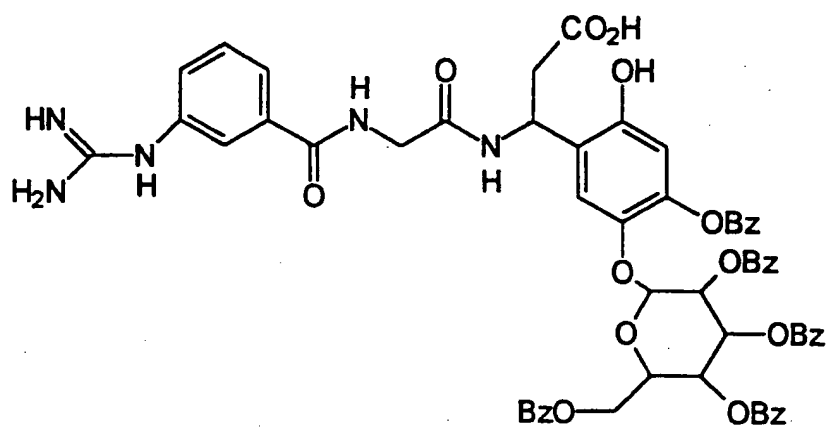
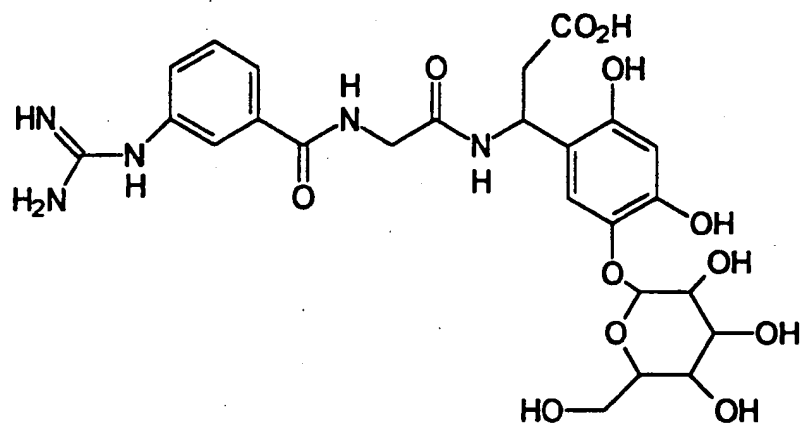
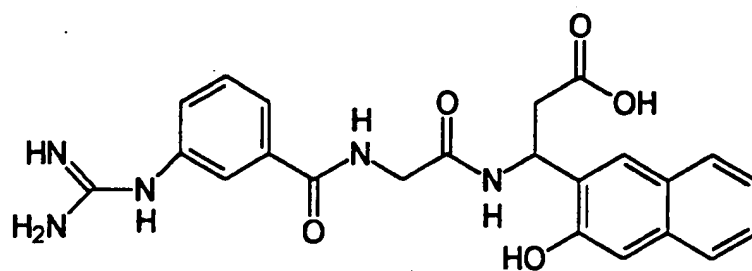
- 793 -



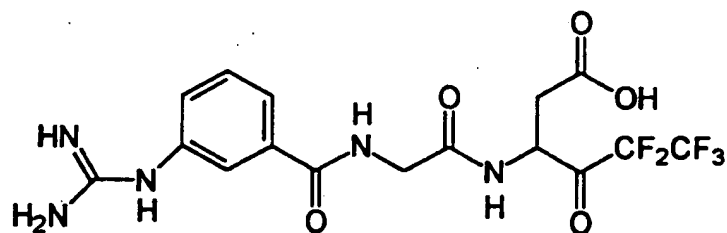
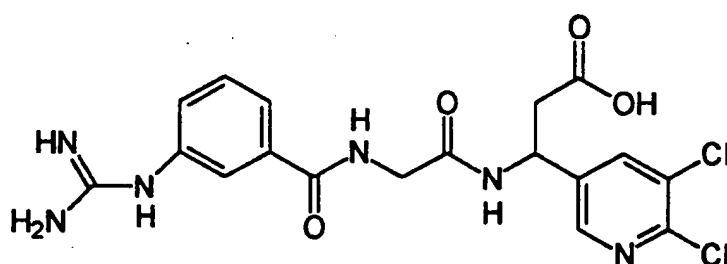
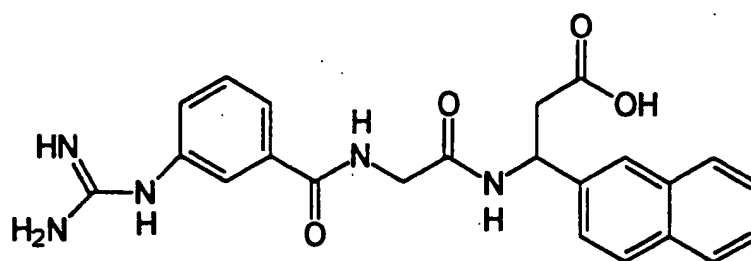
- 794 -



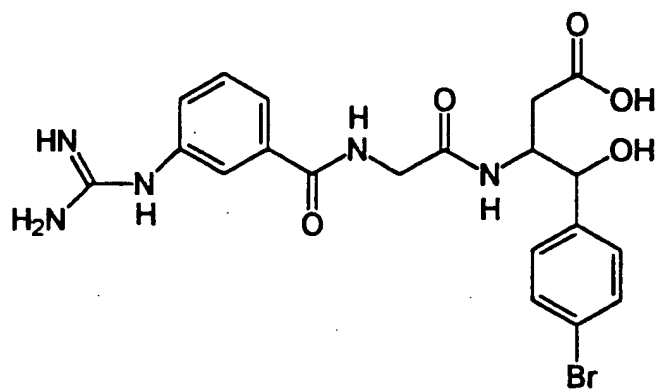
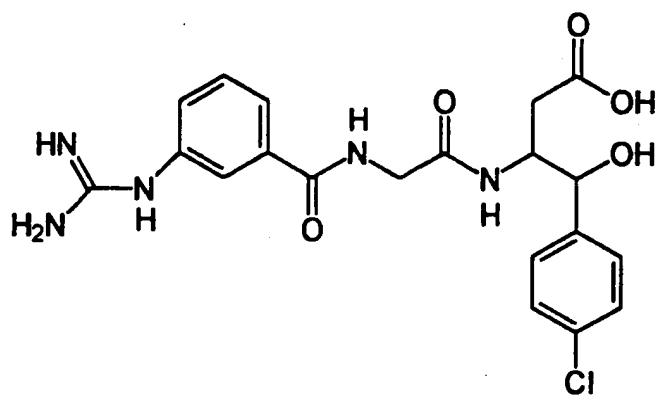
- 795 -



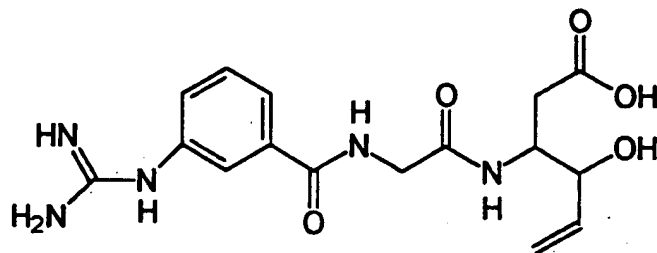
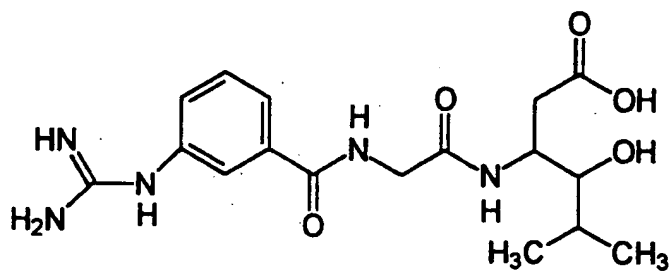
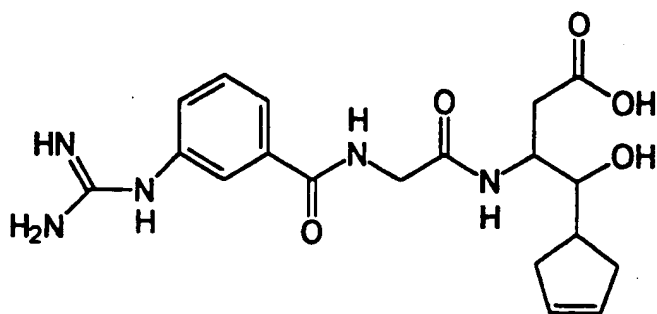
- 796 -



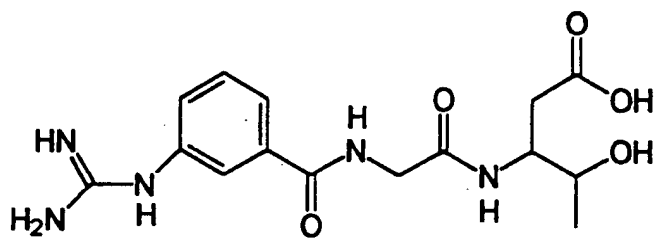
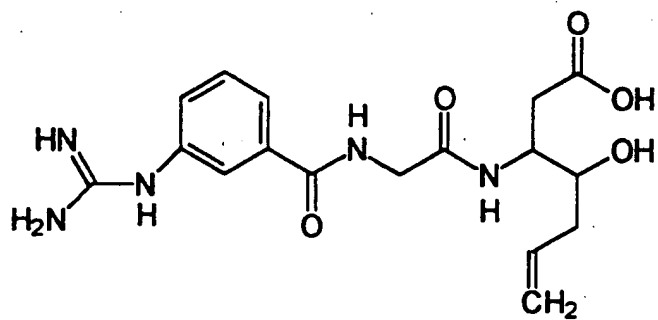
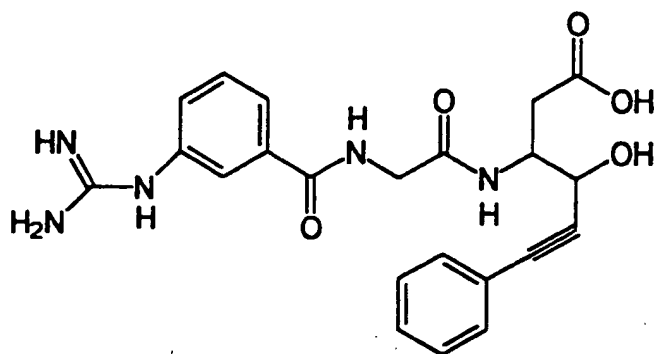
- 797 -



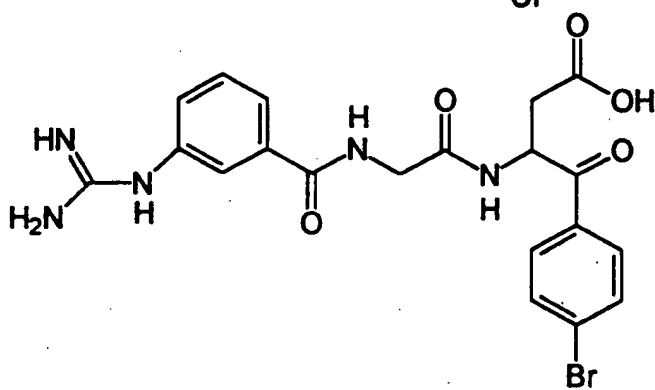
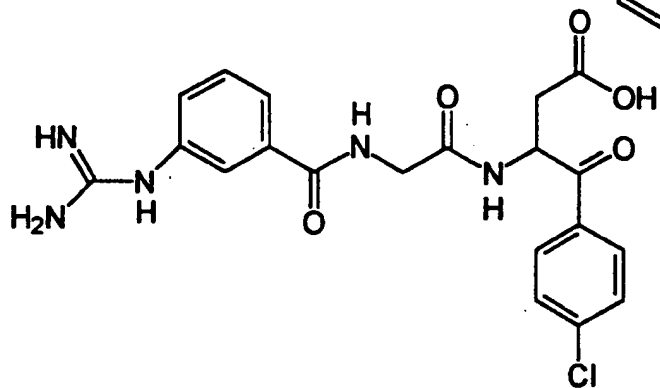
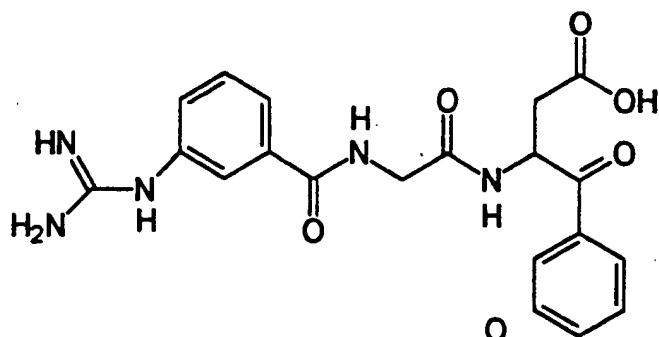
- 798 -



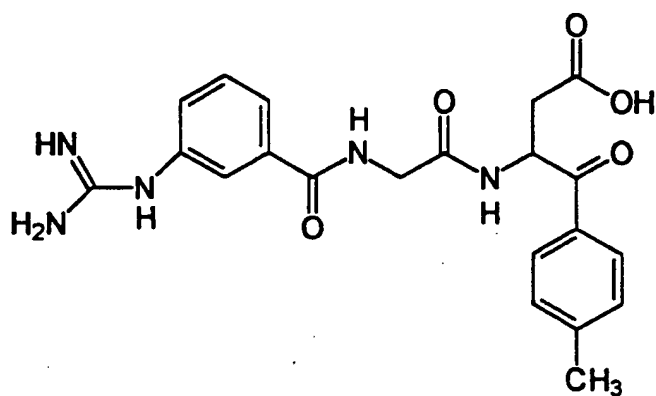
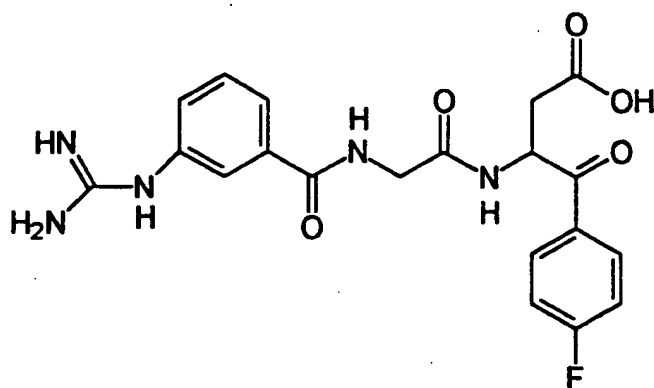
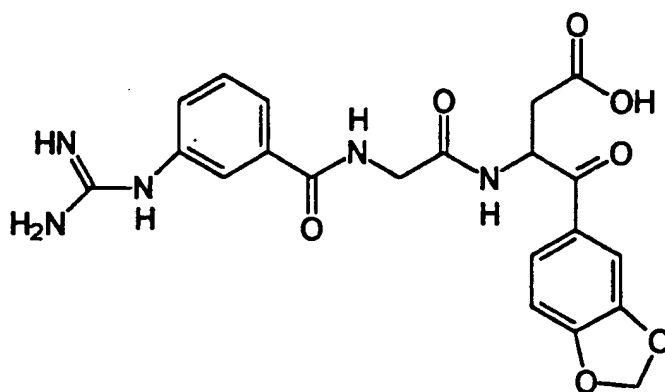
- 799 -



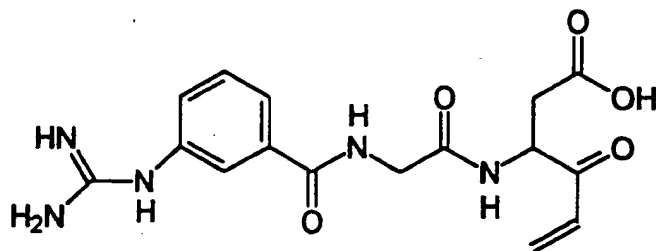
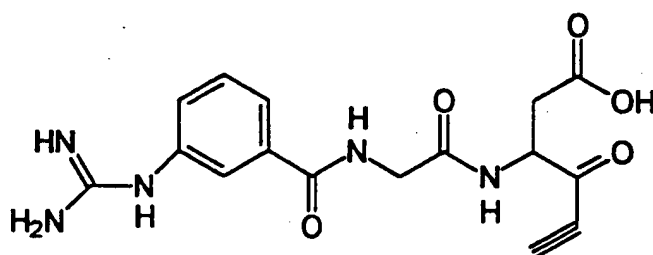
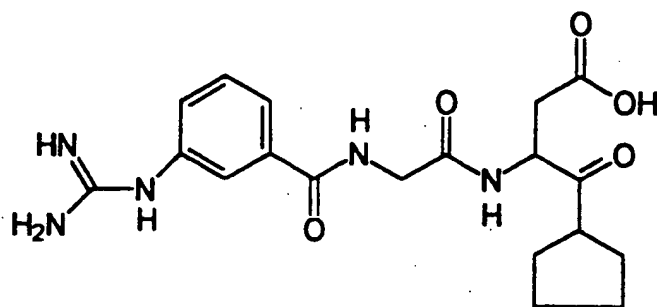
- 800 -



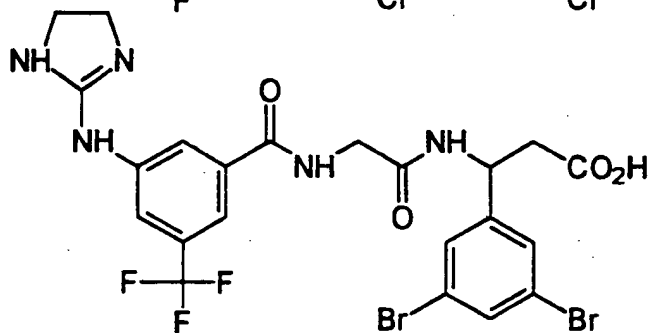
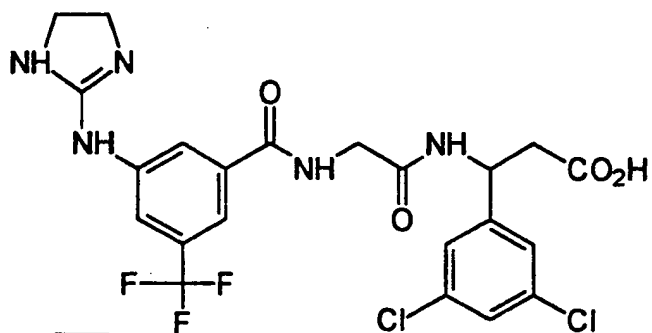
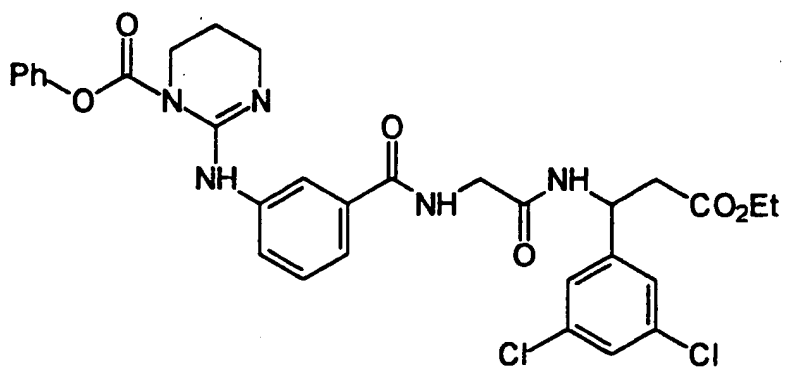
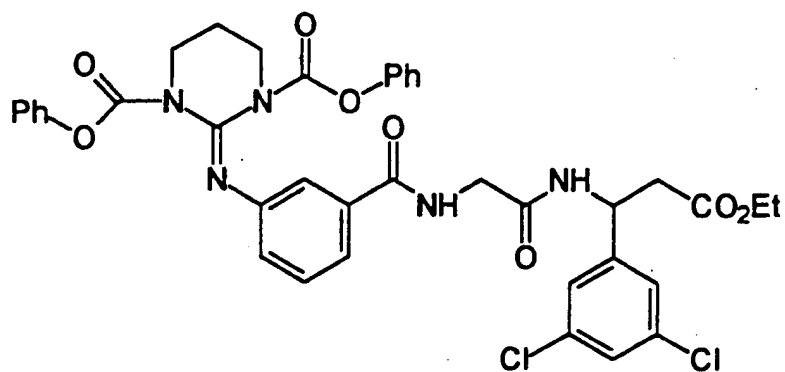
- 801 -



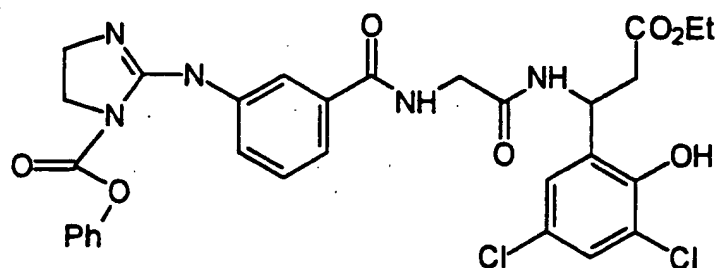
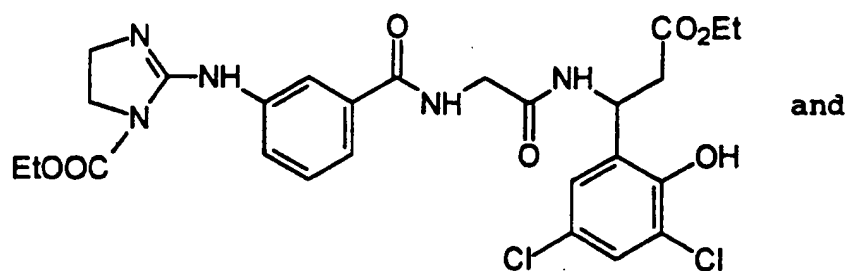
- 802 -



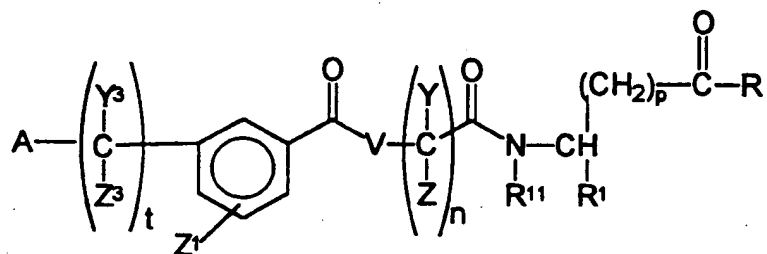
- 803 -



- 804 -

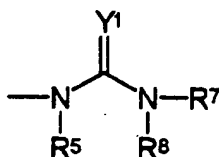


21. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula



or a pharmaceutically acceptable salt thereof,
wherein

A is



wherein Y¹ is selected from the group consisting of N-R², O, and S;

- 805 -

R^2 is selected from the group consisting of H; alkyl; aryl; hydroxy; alkoxy; cyano; nitro; amino; alkenyl; alkynyl; amido; alkylcarbonyl; arylcarbonyl; alkoxycarbonyl; aryloxycarbonyl; haloalkylcarbonyl; haloalkoxycarbonyl; alkylthiocarbonyl; arylthiocarbonyl; acyloxymethoxycarbonyl; alkyl optionally substituted with one or more substituent selected from lower alkyl, halogen, hydroxyl, haloalkyl, cyano, nitro, carboxyl, amino, alkoxy, aryl or aryl optionally substituted with one or more halogen, haloalkyl, lower alkyl, alkoxy, cyano, alkylsulfonyl, alkylthio, nitro, carboxyl, amino, hydroxyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles, or fused monocyclic heterocycles; aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, hydroxy, lower alkyl, alkoxy, methylenedioxy, ethylenedioxy, cyano, nitro, alkylthio, alkylsulfonyl, sulfonic acid, sulfonamide, carboxyl derivatives, amino, aryl, fused aryl, monocyclic heterocycles and fused monocyclic heterocycle; monocyclic heterocycles; and monocyclic heterocycles optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, amino, nitro, hydroxy, carboxyl derivatives, cyano, alkylthio, alkylsulfonyl, sulfonic acid, sulfonamide, aryl or fused aryl; or

R^2 taken together with R^1 forms a 4-12 membered dinitrogen containing heterocycle optionally substituted with one or more substituent selected from the group consisting of lower alkyl, hydroxy, keto, alkoxy, halo, phenyl, amino, carboxyl or carboxyl ester, and fused phenyl;

- 806 -

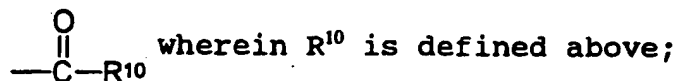
or R^2 taken together with R^7 forms a 5 membered heteroaromatic ring optionally substituted with one or more substituent selected from lower alkyl, phenyl and hydroxy;

or R^2 taken together with R^7 forms a 5 membered heteroaromatic ring fused with a phenyl group;

R^7 (when not taken together with R^2) and R^8 are independently selected from the group consisting of H; alkyl; alkenyl; alkynyl; aralkyl; amino; alkylamino; hydroxy; alkoxy; arylamino; amido, alkylcarbonyl, arylcarbonyl; alkoxycarbonyl; aryloxy; haloalkylcarbonyl; aryloxy; haloalkoxycarbonyl; alkylthiocarbonyl; arylthiocarbonyl; acyloxymethoxycarbonyl; cycloalkyl; bicycloalkyl; aryl; acyl; benzoyl; alkyl optionally substituted with one or more substituent selected from lower alkyl, halogen, hydroxy, haloalkyl, cyano, nitro, carboxyl derivatives, amino, alkoxy, thio, alkylthio, sulfonyl, aryl, aralkyl, aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, carboxyl derivatives, aryloxy, amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethyl, sulfonyl, alkylsulfonyl, haloalkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles, fused monocyclic heterocycles; aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, methyl nedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, carboxyl derivatives, aryloxy, amido, acylamino,

- 807 -

amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethylsulfonyl, alkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles, or fused monocyclic heterocycles; monocyclic heterocycles; monocyclic heterocycles optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, aryloxy, amino, nitro, hydroxy, carboxyl derivatives, cyano, alkylthio, alkylsulfonyl, aryl, fused aryl; monocyclic and bicyclic heterocyclicalkyls; $-SO_2R^{10}$ wherein R^{10} is selected from the group consisting of alkyl, aryl and monocyclic heterocycles, all optionally substituted with one or more substituent selected from the group consisting of halogen, haloalkyl, alkyl, alkoxy, cyano, nitro, amino, acylamino, trifluoroalkyl, amido, alkylaminosulfonyl, alkylsulfonyl, alkylsulfonylamino, alkylamino, dialkylamino, trifluoromethylthio, trifluoroalkoxy, trifluoromethylsulfonyl, aryl, aryloxy, thio, alkylthio, and monocyclic heterocycles; and



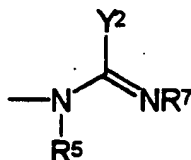
or NR^7 and R^8 taken together form a 4-12 membered mononitrogen containing monocyclic or bicyclic ring optionally substituted with one or more substituent selected from lower alkyl, carboxyl derivatives, aryl or hydroxy and wherein said ring optionally contains a heteroatom selected from the group consisting of O, N and S;

R^5 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, benzyl, and phenethyl;

- 808 -

or

A is



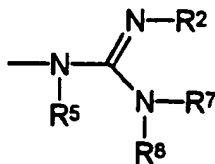
wherein Y^2 is selected from the group consisting of alkyl; cycloalkyl; bicycloalkyl; aryl; monocyclic heterocycles; alkyl optionally substituted with aryl which can also be optionally substituted with one or more substituent selected from halo, haloalkyl, alkyl, nitro, hydroxy, alkoxy, aryloxy, aryl, or fused aryl; aryl optionally substituted with one or more substituent selected from halo, haloalkyl, hydroxy, alkoxy, aryloxy, aryl, fused aryl, nitro, methylenedioxy, ethylenedioxy, or alkyl; alkynyl; alkenyl; $-\text{S}-\text{R}^9$ and $-\text{O}-\text{R}^9$ wherein R^9 is selected from the group consisting of H; alkyl; aralkyl; aryl; alkenyl; and alkynyl; or R^9 taken together with R^7 forms a 4-12 membered mononitrogen and monosulfur or monooxygen containing heterocyclic ring optionally substituted with lower alkyl, hydroxy, keto, phenyl, carboxyl or carboxyl ester, and fused phenyl; or R^9 taken together with R^7 is thiazole; oxazole; benzoxazole; or benzothiazole; and

R^5 and R^7 are as defined above;

or Y^2 (when Y^2 is carbon) taken together with R^7 forms a 4-12 membered mononitrogen containing ring optionally substituted with alkyl, aryl or hydroxy;

- 809 -

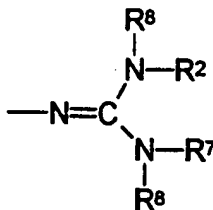
or A is



where R^2 and R^7 taken together form a 5-8 membered dinitrogen containing heterocycle optionally substituted with one or more substituent selected from the group consisting of lower alkyl, hydroxy, keto, phenyl, or carboxyl derivatives; and R^8 is selected from the group consisting of alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxy carbonyl, haloalkylcarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl, or acyloxymethoxycarbonyl; and

R^5 is defined as above

or A is



where R^2 and R^7 taken together form a 5-8 membered dinitrogen containing heterocycle optionally substituted with hydroxy, keto, phenyl, or alkyl; and

R^8 are both selected from the group consisting of alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxy carbonyl, haloalkylcarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl and acyloxymethoxycarbonyl;

- 810 -

Z¹ is one or more substituent s lected from th group consisting of H; alkyl; hydroxy; alkoxy; aryloxy; halogen; haloalkyl; haloalkoxy; nitro; amino; alkylamino; acylamino; dialkylamino; cyano; alkylthio; alkylsulfonyl; carboxyl derivatives; trihaloacetamide; acetamide; aryl; fused aryl; cycloalkyl; thio; monocyclic heterocycles; fused monocyclic heterocycles; and A, wherein A is defined above;

V is selected from the group consisting of -N-(R⁶)- wherein R⁶ is selected from the group consisting of H; lower alkyl; cycloalkyl; aralkyl; aryl; and monocyclic heterocycles; or R⁶ taken together with Y, forms a 4-12 membered mononitrogen containing ring;

Y, Y³, Z and Z³ are independently selected from the group consisting of hydrogen; alkyl; aryl; and cycloalkyl; or Y and Z taken together form a cycloalkyl; or Y³ and Z³ taken together form a cycloalkyl;

n is an integer 1, 2, or 3;

t is an integer 0, 1, or 2;

p is an integer 0, 1, 2, or 3;

R is X-R³ wherein X is selected from the group consisting of O, S and NR⁴, wherein R³ and R⁴ are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; haloalkyl; aryl; arylalkyl; sugars; steroids; polyalkyl thers; alkylamido; alkyl N,N-dialkylamido; pivaloyloxymethyl; and in the case

- 811 -

of the free acid, all pharmaceutically acceptable salts thereof;

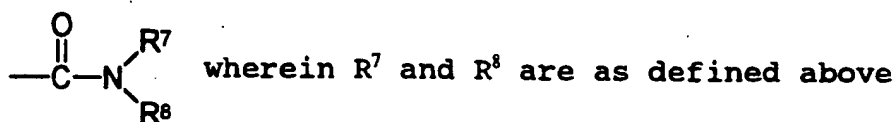
R¹ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; carboxyl derivatives; haloalkyl; monocyclic heterocycles; monocyclic heterocycles optionally substituted with alkyl, halogen, haloalkyl, cyano, hydroxy, aryl, fused aryl, nitro, alkoxy, aryloxy, alkylsulfonyl, arylsulfonyl, sulfonamide, thio, alkylthio, carboxyl derivatives, amino, amido;

alkyl optionally substituted with one or more of halo, haloalkyl, hydroxy, alkoxy, aryloxy, thio, alkylthio, alkynyl, alkenyl, alkyl, arylthio, alkylsulfoxide, alkylsulfonyl, arylsulfoxide, arylsulfonyl, cyano, nitro, amino, alkylamino, dialkylamino, alkylsulfonamide, arylsulfonamide, acylamide, carboxyl derivatives, sulfonamide, sulfonic acid, phosphonic acid derivatives, phosphinic acid derivatives, aryl, arylthio, arylsulfoxide, or arylsulfone all optionally substituted on the aryl ring with halo, alkyl, haloalkyl, cyano, nitro, hydroxy, carboxyl derivatives, alkoxy, aryloxy, amino, alkylamino, dialkylamino, amido, aryl, fused aryl, monocyclic heterocycles; and fused monocyclic heterocycles, monocyclic heterocyclicthio, monocyclic heterocyclicsulfoxide, and monocyclic heterocyclic sulfone, which can be optionally substituted with halo, haloalkyl, nitro, hydroxy, alkoxy, fused aryl, or alkyl;

alkylcarbonyl, haloalkylcarbonyl, and arylcarbonyl;

- 812 -

aryl optionally substituted in one or more positions with halo, haloalkyl, alkyl, alkoxy, aryl xy, methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, acyloxy, carboxyl derivatives, carboxyalkoxy, amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethylsulfonyl, alkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles and fused monocyclic heterocycles; and



and provided that taken together with the nitrogen, R⁷ and R⁸ comprise an amino acid;

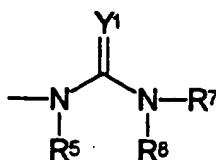
and

R¹¹ is selected from the group consisting of H, alkyl, aralkyl, alkenyl, alkynyl, haloalkyl or haloalkynyl or R¹¹ taken together with Y forms a 4-12 membered mononitrogen containing ring; and

a pharmaceutically acceptable carrier.

22. A pharmaceutical composition according to Claim 21 wherein

A is



wherein Y¹ is selected from the group consisting of N-R², O, and S;

- 813 -

R^2 is selected from the group consisting of H, alkyl, aryl, substituted alkyl, hydroxy, alkoxy, alkylcarbonyl, cyano, nitro, amino and monocyclic heterocycles, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl, acyloxymethoxycarbonyl; or R^2 taken together with R^7 forms a 4-12 membered ring;

R^5 , R^7 , R^8 are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, bicycloalkyl substituted alkyl, arylalkyl, aryloxy, hydroxy, alkoxy, amino, alkylamino, arylamino, amido, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkylcarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl, acyloxymethoxycarbonyl, substituted phenyl, arylacyl, monocyclic and bicyclic heterocycles, monocyclic and bicyclic heterocyclicalkyl and $-SO_2R^{10}$ wherein R^{10} is selected from the group consisting of alkyl, amino and aryl which are all optionally substituted with one or more substituent selected from the group consisting of acylamino, amino, carbonyl, cyano, nitro, alkoxy, halo, alkyl, trifluoroalkyl, amido, alkylaminosulfonyl, alkylsulfonyl, alkylsulfonylamino, alkylamino, dialkylamino, aryloxy, thio, trifluoromethylthio, trifluoroalkoxy, and trifluoromethylsulfonyl or $-NR^7$ and R^8 taken together form a 4-12 membered ring wherein said ring optionally contains a heteroatom selected from the group consisting of O, N, and S wherein said ring is optionally substituted.

- 814 -

23. A pharmaceutical composition according to Claim 22
wh rein

V is $-N(R^6)-$ wherein R^6 is selected from the group
consisting of H and lower alkyl;

n is 1;

t is 0 or 1; and

p is 0, 1 or 2.

24. A pharmaceutical composition according to Claim 23
wherein the compound is selected from the group
consisting of

(±)ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]pyridine-3-propanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]pyridine-3-
propanoic acid;

(±)ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]benzenepropanoate;

(±) β -[[2-[[[3-
[(aminoiminomethyl)amino]phenyl]carbonyl]-
amino]acetyl]amino]benzenepropanoic acid;

(±)ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-1,3-
benzodioxole-5-propanoate;

- 815 -

- (±)β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-1,3-benzodioxole-5-propanoic acid;
- (±)ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]-naphthalen-1-yl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;
- (±)β-[[2-[[[3-[(aminoiminomethyl)-amino]-naphthalen-1-yl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoic acid;
- (±)ethyl β-[[1-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]-1-cyclopropyl]-carbonyl]amino]pyridine-3-propanoate;
- (±)β-[[1-[[[3[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]cycloprop-1-yl]carbonyl]-amino]pyridine-3-propanoic acid;
- (±)ethyl β-[[2-[[[3-[[imino[(phenylmethyl)amino]-methyl]amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;
- (±)β-[[2-[[[3-[[imino[(phenylmethyl)amino]methyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;
- β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;
- 3S-[[2-[[[3-(aminocarbonylamino)phenyl]-carbonyl]amino]acetyl]amino]-4-pentynoic acid;
- ethyl 3S-[[2-[[[3-(aminocarbonylamino)phenyl]-carbonyl]amino]acetyl]amino]-4-pentynoate;

- 816 -

β S-[[2-[[[3-[(aminoiminomethyl)amino]-2,5,6-trifluorophenyl]carbonyl]amino]acetyl]-amino]-4-pentynoic acid;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

ethyl (\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-[1,1'-biphenyl]-4-propanoic acid;

ethyl (\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-[1,1'-biphenyl]-4-propanoate;

(\pm) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-naphthalene-1-carboxylic acid;

- 817 -

methyl (\pm) β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
naphthalene-1-carboxylate;

(\pm) 3-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]-2-oxopyrrolidine-1-
propanoic acid;

3R-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-pentynoic acid;

ethyl 3R-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-pentynoate;

3S-[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]-4-pentynoic acid;

ethyl 3S-[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]-4-pentynoate;

3S-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-pentynoic acid;

β -[[2-[[[3-(aminocarbonylamino)phenyl]-
carbonyl]amino]acetyl]amino]pyridine-
3-propanoic acid;

ethyl β -[[2-[[[3-(aminocarbonylamino)phenyl]-
carbonyl]amino]acetyl]amino]pyridine-3-propanoate;

(\pm) β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

- 818 -

(±) ethyl β-[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

(±) ethyl β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]-amino]furan-2-propanoate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-furan-3-propanoic acid;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]-amino]acetyl]amino]pentanedioic acid;

bismethyl ester 3-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]-amino]acetyl]amino]pentanedioate;

(±) hydrogen methyl 3-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]-amino]pentanedioate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-furan-2-propanoic acid;

ethyl (±) β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]furan-2-propanoate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-naphthalene-2-propanoic acid;

(±) methyl β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-thiophene-3-propanoate;

- 819 -

ethyl 3S-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
4-pentynoate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
thiophene-3-propanoic acid;

(±) 2-[3-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-4-
carboxybutyl]thio]benzoic acid;

(±) 2-[3-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-4-
carboxybutyl]sulfonyl]benzoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
thiophene-2-propanoic acid;

(±) methyl 2-[3-[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-4-
carboxybutyl]thio]benzoate;

(±) methyl 3-[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
5-[(4-methylphenyl)thio]pentanoate;

(±) methyl 3-[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
4-[(4-methylphenyl)sulfonyl]amino]butanoate;

3-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-4-[(4-
methylphenyl)sulfonyl]amino]butanoic acid;

- 820 -

(±) 3-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-5-[(4-methylphenyl)thio]pentanoic acid;

(±) 3-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-5-[(4-methylphenyl)sulfonyl]pentanoic acid;

3S-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-4-(phenylthio)butanoic acid;

3R-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-pentynoic acid;

ethyl 3R-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-pentynoate;

2-[[2S-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-2-(carboxymethyl)ethyl]sulfonyl]benzoic acid;

3S-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-pentynoic acid;

ethyl 3S-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-pentynoate;

2-[[2S-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-2-(carboxymethyl)ethyl]thio]benzoic acid;

- 821 -

(±) thyl β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]methylamino]acetyl]-amino]pyridine-3-propanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]methylamino]acetyl]amino]pyridine-3-propanoic acid;

(±) ethyl β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]-1-oxopropyl]-amino]pyridine-3-propanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]-1-oxopropyl]-amino]pyridine-3-propanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-4-methylphenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoic acid;

(±) β -[[2-[[[3-[[[aminoiminomethyl)amino]-methyl]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoic acid;

3S-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4-hydroxybutanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]-amino]-2-hydroxybenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-2-hydroxy-5-methylbenzenepropanoic acid;

- 822 -

(±) 3-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-[(2-hydroxyethyl)amino]-4-ox butanoic acid;

2S-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3-carboxypropyl 2-aminobenzoate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-1,4-benzodioxin-6-propanoic acid;

N-[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]-β-alanine, ethyl ester;

N-[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]-β-alanine;

(±) ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-quinoline-3-propanoate;

β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-quinoline-3-propanoic acid;

N-[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]-β-alanine, ethyl ester;

3-[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]amino]propanoic acid;

(±) ethyl β-[[2-[[[3-[[[(phenylmethyl)amino]-carbonyl]amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoate;

- 823 -

(±) β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(phenylamino)carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate;

β -[[2-[[[3-[[[(phenylamino)carbonyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-(aminocarbonylamino)-
phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate;

β -[[2-[[[3-(aminocarbonylamino)phenyl]-
carbonyl]amino]acetyl]amino]pyridine-3-
propanoic acid;

ethyl β -[[2-[[[3-[[[(4-methylphenyl)sulfonyl]-
amino]carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]pyridine-3-propanoate;

β -[[2-[[[3-[[[(4-methylphenyl)sulfonyl]amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(aminothioxomethyl)-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoate;

β -[[2-[[[3-[(aminothioxomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]pyridine-
3-propanoic acid;

- 824 -

ethyl β -[[2-[[[3-[(aminothioxomethyl)amino]-
phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoate;

β -[[2-[[[3-[(aminothioxomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoic acid;

ethyl β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoate;

β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoic acid;

ethyl β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]-1,3-benzodioxole-5-propanoate;

β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
1,3-benzodioxole-5-propanoic acid;

ethyl β -[[2-[[[3-3-[[[(phenylamino)carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
1,3-benzodioxole-5-propanoate;

β -[[2-[[[3-3-[[[(phenylamino)carbonyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-1,3-
benzodioxole-5-propanoic acid;

β -[[2-[[[3-[[[(4-(aminosulfonyl)phenylmethyl]-
amino]carbonyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]pyridine-
3-propanoic acid;

- 825 -

β -[[2-[[[3-[[[(3-pyridinylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

β -[[2-[[[3-[[[(2-carboxyethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

β -[[2-[[[3-[[[(2-phenylethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

β -[[2-[[[3-[[[(1-naphthalenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-4-
chlorophenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-4-
chlorophenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoic acid;

β -[[2-[[[5-[(aminoiminomethyl)amino]-2-chlorophenyl]-
carbonyl]amino]acetyl]amino]benzenepropanoic acid;

ethyl β -[2-[[[3-[[amino(aminocarbonyl)-
imino]methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]-3,5-
dichlorobenzenepropanoate;

β -[[2-[[[3-[[amino(aminocarbonyl)imino]-
methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]-3,5-dichlorobenzene-
propanoic acid;

- 826 -

[(dimethylamino)carbonyl]methyl β -
 [[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
 carbonyl]amino]acetyl]amino]-3,5-
 dichlorobenzenepropanoate;

1,1-dimethylethyl 3,5-dichloro- β -[[2-[[[3[[[(ethoxy-
 carbonyl)amino] [(ethoxycarbonyl)imino]methyl]amino]-
 phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

3,5-dichloro- β -[[2-[[[3-[[[(ethoxycarbonyl)-
 amino] [(ethoxycarbonyl)imino]methyl]-
 amino]-phenyl]carbonyl]amino]acetyl]-
 amino]benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-4-
 chlorophenyl]carbonyl]amino]acetyl]amino-
 3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-4-
 chlorophenyl]carbonyl]amino]acetyl]amino]-
 3,5-dichlorobenzenepropanoic acid;

ethyl 3S-[[2-[[[3-[[amino[(aminocarbonyl)imino]-
 methyl]amino]phenyl]carbonyl]amino]acetyl]-
 amino]-4-pentynoate;

3S-[[2-[[[3-[[amino[(aminocarbonyl)imino]-
 methyl]amino]phenyl]carbonyl]amino]-
 acetyl]amino]-4-pentynoic acid;

ethyl 3S-[[2-[[[3-[(aminoiminomethyl)-
 amino]-4-chlorophenyl]carbonyl]amino]-
 acetyl]amino]-4-pentynoate;

3S-[[2-[[[3-[(aminoiminomethyl)amino]-4-
 chlorophenyl]carbonyl]amino]acetyl]-
 amino]-4-pentynoic acid;

- 827 -

- (±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,4-dichlorobenzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3,4-dichlorobenzenepropanoic acid;
- (±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)carbonyl]amino]acetyl]amino]-3,4-dichlorobenzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;
- (±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-2,5-dimethylbenzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2,5-dimethylbenzenepropanoic acid;
- (±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-chlorobenzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3-chlorobenzenepropanoic acid;

- 828 -

- (±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-bromob nzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-bromobenzenepropanoic acid;
- (±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-bromobenzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-bromobenzenepropanoic acid;
- (±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethylbenzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethylbenzenepropanoic acid;
- (±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethoxybenzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethoxybenzenepropanoic acid;
- (±) (2,2-dimethyl-1-oxopropoxy)methyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenz nepropanoate;

- 829 -

- (±) β -[[2-[[[3-[[[(aminocarbonyl)imino)-methylamino)methyl]amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminothioxomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,4-dibromobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3-fluoro-5-(trifluoromethyl)benzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-fluorobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3-bromo-5-methylbenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3-bromo-5-chlorobenzenepropanoic acid;

- 830 -

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]-amino]-3-bromo-5-chlorobenzenepropanoic acid;

(±) [2-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]-ethyl] β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-iodobenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2-hydroxy-4-methoxybenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-5-hydroxy-4-methoxybenzofuran-6-propanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-9H-fluorene-2-propanoic acid;

ethyl(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-9H-fluorene-2-propanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-dichloro-2-hydroxybenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2-hydroxy-5-nitrobenzenepropanoic acid;

- 831 -

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromo-2-hydroxybenzenepropanoic acid;

ethyl(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromo-2-hydroxybenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-5-bromo-2-hydroxybenzenepropanoic acid;

ethyl(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-5-bromo-2-hydroxybenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-cyclohexanepropanoic acid;

ethyl(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-cyclohexanepropanoate;

ethyl(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichloro-2-hydroxybenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-5-chloro-2-hydroxybenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-chloro-2-hydroxybenzenepropanoic acid;

- 832 -

(±) 5-amino-β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-2-hydroxybenzenepropanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromopyridine-3-propanoic acid;

ethyl(±) β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromopyridine-3-propanoate;

3,5-dichloro-β-[[2-[[[3-[[[(ethoxycarbonyl)amino]-thioxomethyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

3,5-dichloro-β-[[2-[[[3-[[[(ethoxycarbonyl)amino]-iminomethyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino][1,1'-biphenyl]-3-propanoic acid;

1,1-dimethylethyl β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino][1,1'-biphenyl]-3-propanoate;

β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino][pyrimidine-5-propanoic acid;

1,1-dimethylethyl β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-[pyrimidine-5-propanoate;

β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-methylthiophene-2-propanoic acid;

- 833 -

1,1-dimethylethyl β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3-methylthiophene-2-propanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3-(methylthio)-benzenepropanoic acid;

1,1-dimethylethyl (\pm) β -[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3-(methylthio)benzenepropanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-6-methylpyridine-2-propanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3-(methylsulfonyl)-benzenepropanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-diethoxybenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]-carbonyl]amino]acetyl]amino]-3,5-diethoxybenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-4-bromothiophene-2-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-4-bromothiophene-2-propanoate;

- 834 -

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl-carbonyl]amino]acetyl]amino]-5-chlorothiophene-2-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl-carbonyl]amino]acetyl]amino]-5-chlorothiophene-2-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-1H-pyrazole-3-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-1H-pyrazole-3-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-5-methylthiophene-2-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-5-methylthiophene-2-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2,3,5-trichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2,3,5-trichlorobenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2(carboxymethoxy)-benzenepropanoic acid;

- 835 -

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-2(carboxymethoxy)-
benzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-4-methoxy-1,3-
benzodioxole-6-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-methoxy-1,3-
benzodioxole-6-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-5-bromo-
2-methoxybenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-5-bromo-
2-methoxybenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-6-chloro-
1,3-benzodioxole-5-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-6-chloro-
1,3-benzodioxole-5-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzofuran-2-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzofuran-2-propanoate;

- 836 -

β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-3-
(carboxymethoxy)benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-3-
(carboxymethoxy)benzenepropanoate;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4,4,4-
trifluorobutanoic acid;

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4,4,4-
trifluorobutanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3-bromo-4,5-
dimethoxybenzenepropanoic acid;

ethyl(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3-bromo-4,5-
dimethoxybenzenepropanoate;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-
methylpentanoic acid;

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-
methylpentanoate;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
phenyl]carbonyl]amino]acetyl]amino]-
pentanoic acid;

- 837 -

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-phenyl]carbonyl]amino]acetyl]amino]-pentanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-5-bromo-3-chloro-2-hydroxybenzene-propanoic acid;

β -[[2-[[[3-[[[(4-pyridinylmethyl)amino]-carbonyl]amino]phenyl]carbonyl]amino]-acetyl]amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(4-pyridinylmethyl)amino]-carbonyl]amino]phenyl]carbonyl]amino]-acetyl]amino]pyridine-3-propanoate;

3,5-dichloro- β -[[2-[[[3-[[[(4-pyridinylmethyl)-amino]carbonyl]amino]phenyl]carbonyl]amino]-acetyl]amino]benzenepropanoic acid;

ethyl 3,5-dichloro- β -[[2-[[[3-[[[(4-pyridinylmethyl)-amino]carbonyl]amino]phenyl]carbonyl]amino]-acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[[[(2-pyridinylmethyl)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(2-pyridinylmethyl)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate;

3,5-dichloro- β -[[2-[[[3-[[[(phenylmethyl)amino]-carbonyl]amino]phenyl]carbonyl]amino]-acetyl]amino]benzenepropanoic acid;

- 838 -

ethyl 3,5-dichloro- β -[[2-[[[3-[[[(phenylmethyl)amino]-carbonyl]amino]phenyl]carbonyl]amino]-acetyl]amino]benzenepropanoate;

3-chloro- β -[[2-[[[3-[[[(phenylmethyl)amino]-carbonyl]amino]phenyl]carbonyl]amino]-acetyl]amino]benzenepropanoic acid;

ethyl 3-chloro- β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]amino]phenyl]carbonyl]amino]-acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[[[(1-phenylethyl)amino]carbonyl]amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(1-phenylethyl)amino]carbonyl]amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoate;

β -[[2-[[[3-[[[(1H-benzimidazol-2-yl)-methyl]amino]carbonyl]amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-[[[(1H-benzimidazol-2-yl)-methyl]amino]carbonyl]amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]amino]carbonyl]amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]amino]carbonyl]amino]phenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoate;

- 839 -

3-[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]-
amino]carbonyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]butanoic acid;

ethyl 3-[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]-
amino]carbonyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]butanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-bis(1-methyl-
ethoxy)benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-bis(1-methyl-
ethoxy)benzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dibromo-4-
hydroxybenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dibromo-4-
hydroxybenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dichloro-4-
hydroxybenzenepropanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dichloro-4-
hydroxybenzenepropanoate;

β -[[2-[[[5-[(aminoiminomethyl)amino]-2-
hydroxyphenyl]carbonyl]amino]acetyl]amino]-
-3,5-dichlorobenzenepropanoic acid;

- 840 -

ethyl β -[[2-[[[5-[(aminoiminomethyl)amino]-2-hydroxyphenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[(phenoxyamino)carbonyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(phenoxyamino)carbonyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate;

β -[[2-[[[3-[[[(phenylamino)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(phenylamino)amino]carbonyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-5-[(3,5-dichlorophenyl)amino]-5-oxopentanoic acid;

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-5-[(3,5-dichlorophenyl)amino]-5-oxopentanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxyphenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxyphenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate;

- 841 -

β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxy-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxy-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3,5-bis[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3,5-bis[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoroacetyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoroacetyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-(acetylamino)-5-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-(acetylamino)-5-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

(\pm) 3,5-dichloro- β -[[2-[[[3-[(methylamino)(methylimino)methyl]amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

- 842 -

(±) 3,5-dichloro-β-[[2-[[[3-
[[(thylamino)(methylimino)methyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoic acid;

(±) 3,5-dichloro-β-[[2-[[[3-[[[(1-
methylethyl)amino](methylimino)methyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoic acid;

(±) β-[[2-[[[3-[[(ethylamino)-
(methylimino)methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]-4-fluorobenzene-
propanoic acid;

(±) 4-fluoro-β-[[2-[[[3-[[[(4-
pyridinylmethyl)amino](methylimino)methyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoic acid;

β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-
fluorobenzenepropanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
1H-imidazole-2-propanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-2,3,4,6-
tetrafluorobenzenepropanoic acid;

β-[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
-5-bromothiophene-2-propanoic acid;

- 843 -

β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-2-
mercaptobenzenepropanoic acid;

and

(\pm) β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-5-
chloro-2-mercaptobenzenepropanoic acid.

25. A pharmaceutical composition according to Claim 23
wherein Y¹ is N-R² and R² is cyano.

26. A pharmaceutical composition according to Claim 25
wherein the compound is selected from the group
consisting of

phenylmethyl β -[[2-[[[3-[(cyanoimino)phenylmethyl-
amino)methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

phenylmethyl β -[[2-[[[3-[(cyanoimino)-
methyldamino)methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

phenylmethyl β -[[2-[[[3-[(cyanoimino)-
(amino)methyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoate;

β -[[2-[[[3-[(cyanoimino)(ethylamino)methyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoate;

β -[[2-[[[3-[(cyanoimino)((phenylmethyl)-
amino)methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]benzenepropanoic acid;

- 844 -

β -[[2-[[[3-[[(cyanoimino) (methylamino) -
methyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoic acid;

β -[[2-[[[3-[[amino (cyanoimino) methyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoic acid;

β -[[2-[[[3-[[(cyanoimino) (ethylamino) -
methyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoic acid;

ethyl 3S-[[2-[[[3-[[(cyanoimino) -
(methylamino) methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]-4-pentynoate;

3S-[[2-[[[3-[[(cyanoimino) (methylamino) -
methyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]-4-pentynoic acid;

ethyl β -[[2-[[[3-[[(cyanoimino) [2-pyridinylmethyl) -
amino]methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[[(cyanoimino) [2-pyridinylmethyl) -
amino]methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoic acid;

ethyl β -[[2-[[[3-[[(cyanoimino) [3-
pyridinylmethyl) amino]methyl]amino]phenyl]-
carbonyl]amino]acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[[(cyanoimino) [3-pyridinylmethyl) -
amino]methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoic acid;

- 845 -

ethyl 3S-[[2-[[[3-[[[(4-(aminosulfonyl)-
phenylmethyl]amino)(cyanoimino)methyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]-4-pentynoate;

3S-[[2-[[[3-[[[(4-(aminosulfonyl)phenylmethyl)-
amino](cyanoimino)methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]-4-pentynoic acid;

ethyl β -[[2-[[[3-[[amino(cyanoimino)methyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-3,5-
dichlorobenzenepropanoate;

β -[[2-[[[3-[[amino(cyanoimino)methyl]amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-
dichlorobenzenepropanoic acid;

(\pm) ethyl 3,5-dichloro- β -[[2-[[[3-[(cyanoimino)-
(methylamino)methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]benzenepropanoate;

(\pm) 3,5-dichloro- β -[[2-[[[3-[(cyanoimino)(methylamino)-
methyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoic acid;

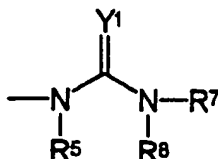
and

ethyl 3-[[2-[[[3-[[amino(cyanoimino)methyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-4-pentynoate.

- 846 -

27. A pharmaceutical composition according to Claim 21
wherein in

A is



wherein Y^1 is N-R^2 ; R^2 taken together with R^7 forms a 4-12 membered ring; and R^8 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, bicycloalkyl substituted alkyl, arylalkyl, aryloxy, hydroxy, alkoxy, amino, alkylamino, arylamino, amido, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkylcarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl, acyloxymethoxycarbonyl, substituted phenyl, arylacyl, monocyclic and bicyclic heterocycles, monocyclic and bicyclic heterocyclicalkyl and $-\text{SO}_2\text{R}^{10}$ wherein R^{10} is selected from the group consisting of alkyl, amino and aryl which are all optionally substituted with one or more substituent selected from the group consisting of acylamino, amino, carbonyl cyano, nitro, alkoxy, halo, alkyl, trifluoroalkyl, amido, alkylaminosulfonyl, alkylsulfonyl, alkylsulfonylamino, alkylamino, dialkylamino, aryloxy, thio, trifluoromethylthio, trifluoroalkoxy, and trifluoromethylsulfonyl or $-\text{NR}^7$ and R^8 taken together form a 4-12 membered ring wherein said ring optionally contains a heteroatom selected from the group consisting of O, N, and S wherein said ring is optionally substituted.

- 847 -

28. A pharmaceutical composition according to Claim 27 wherein

V is -N(R⁶)- wherein R⁶ is selected from the group consisting of H and lower alkyl;

n is 1;

t is 0; and

p is 1.

29. A pharmaceutical composition according to Claim 28 wherein the compound is selected from the group consisting of

(±)ethyl β-[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

(±)β-[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

(±) ethyl β-[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoate;

(±) β-[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

(±) ethyl β-[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]-3,5-dichlorobenzenepropanoate;

- 848 -

(±) β -[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

(±) ethyl 3,5-dichloro- β -[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

(±) 3,5-dichloro- β -[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

(±) 3,5-dibromo- β -[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

(±) 3-bromo-5-chloro- β -[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

(±) [2-[2-[2-(2-hydroxyethoxy)-ethoxy]ethoxy]ethyl] 3,5-dichloro- β -[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

(±) [2-[2-(2-hydroxyethoxy)-ethoxy]ethoxy]ethyl] 3,5-dichloro- β -[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

(±) 3-bromo-5-chloro-2-hydroxy- β -[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

- 849 -

ethyl (±) 3-bromo-5-chloro-2-hydroxy-β-
[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoate;

(±) 3,5-dichloro-2-hydroxy-β-[[2-
[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoic acid;

(±) 3,5-dichloro-β-[[2-[[[3-[(4,5-dihydro-
1H-pyrrolidin-2-yl)amino]phenyl]carbonyl]amino]-
amino]acetyl]amino]-2-hydroxybenzenepropanoic acid;

(±) 3-bromo-5-chloro-β-[[2-[[[3-[(4,5-dihydro-
1H-pyrrolidin-2-yl)amino]phenyl]carbonyl]amino]-
acetyl]amino]-2-hydroxybenzenepropanoic acid;

β-[[2-[[[3-[[5-phenyl-1H-imidazol-2-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

ethyl β-[[2-[[[3-[[5-phenyl-1H-imidazol-2-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate;

(±) ethyl 3,5-dichloro-β-[[2-[[[3-
[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoate;

(±) 3,5-dichloro-β-[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-
dimethylpyrimidin-2-yl)amino]phenyl]carbonyl]-
amino]acetyl]amino]benzenepropanoic acid;

- 850 -

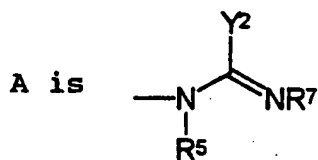
thyl (\pm) 3,5-dichloro-2-hydroxy- β -[[2-[[[3-
[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoate;

(\pm) 3-bromo-5-dichloro-2-hydroxy-
 β -[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-
dimethylpyrimidin-2-yl)amino]phenyl]-
carbonyl]amino]acetyl]amino]benzene-
propanoic acid;

and

ethyl(\pm) 3-bromo-5-dichloro-2-hydroxy- β -[[2-[[[3-
[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-
yl)amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoate.

30. A pharmaceutical composition according to Claim 21 wherein



wherein Y^2 is selected from the group consisting of lower alkyl, substituted alkyl, phenyl, substituted phenyl, cycloalkyl, monocyclic heterocycles, $-\text{S}-\text{R}^9$ and $-\text{O}-\text{R}^9$ wherein R^9 is selected from the group consisting of H, alkyl, substituted alkyl, phenyl, substituted phenyl and monocyclic heterocycles or R^9 taken together with R^7 forms a 4-12 membered ring; or

- 851 -

Y² taken together with R⁷ forms a 4-12 membered ring which is optionally substituted.

31. A pharmaceutical composition according to Claim 30 wherein

Y² taken together with R⁷ forms a 4-12 membered ring which is optionally substituted.

32. A pharmaceutical composition according to Claim 31 wherein

V is -N(R⁶)- wherein R⁶ is selected from the group consisting of H and lower alkyl;

n is 1;

t is 0 or 1; and

p is 1.

33. A pharmaceutical composition according to Claim 32 wherein the compound is selected from the group consisting of

(±) ethyl β-[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

(±) β-[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoic acid;

(±) ethyl β-[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-1,3-benzodioxole-5-propanoate;

- 852 -

- (±) β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-1,3-benzodioxole-5-propanoic acid;
- (±) β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;
- (±) ethyl β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;
- β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;
- (±) ethyl β -[[2-[[[4-chloro-3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]-acetyl]amino]pyridine-3-propanoate;
- (±) β -[[2-[[[4-chloro-3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]-acetyl]amino]pyridine-3-propanoic acid;
- (±) β -[[2-[[[3,5-bis[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoic acid;
- β S-[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]-4-pentynoic acid;
- (±) ethyl β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

- 853 -

(±) β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]-3,5-dichlorobenzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]-3,5-dichlorobenzenepropanoate;

(±) β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

(±) ethyl 3,5-dichloro- β -[[2-[[[3-[(2,3,4,5-tetrahydropyridin-6-yl)amino]phenyl]-carbonyl]amino]acetyl]amino]benzenepropanoate;

(±) 3,5-dichloro- β -[[2-[[[3-[(2,3,4,5-tetrahydropyridin-6-yl)amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoic acid;

(±) 3,5-dichloro-2-hydroxy- β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

and

ethyl(±) 3,5-dichloro-2-hydroxy- β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoate.

- 854 -

34. A pharmaceutical composition according to Claim 30 wherein

Y^2 is selected from the group consisting of lower alkyl, substituted alkyl, phenyl, substituted phenyl, cycloalkyl and monocyclic heterocycles.

35. A pharmaceutical composition according to Claim 34 wherein

V is $-N(R^6)-$ wherein R^6 is selected from the group consisting of H and lower alkyl;

n is 1;

t is 0; and

p is 1.

36. A pharmaceutical composition according to Claim 35 wherein the compound is selected from the group consisting of

(±) ethyl β -[[2-[[[3-[(iminophenylmethyl)-amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

β S-[[2-[[[3-[[imino(1-pyrrolidinyl)methyl]-amino]phenyl]carbonyl]amino]acetyl]-amino]-4-pentynoic acid;

(±) β -[[2-[[[3-[(iminophenylmethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

- 855 -

3,5-dichloro- β -[[2-[[[3-[[imino(1-piperidinyl)methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoic acid;

and

ethyl 3,5-dichloro- β -[[2-[[[3-[[imino(1-piperidinyl)methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoate.

37. A pharmaceutical composition according to Claim 30 wherein Y^2 is $-S-R^9$ or $-O-R^9$ wherein R^9 is selected from the group consisting of H, alkyl, substituted alkyl, phenyl, substituted phenyl and monocyclic heterocycles or R^9 taken together with R^7 forms a 4-12 membered ring.

38. A pharmaceutical composition according to Claim 37 wherein

V is $-N(R^6)-$ wherein R^6 is selected from the group consisting of H, lower alkyl, substituted alkyl, cycloalkyl, aryl, substituted aryl, monocyclic heterocycles and benzyl;

n is 0;

t is 0; and

p is 1 or 2.

39. A pharmaceutical composition according to Claim 38 wherein the compound is selected from the group consisting of

- 856 -

ethyl β -[[2-[[[3-[(4,5-dihydrothiazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

β -[[2-[[[3-[(4,5-dihydrothiazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

β -[[2-[[[3-[(benzoxazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

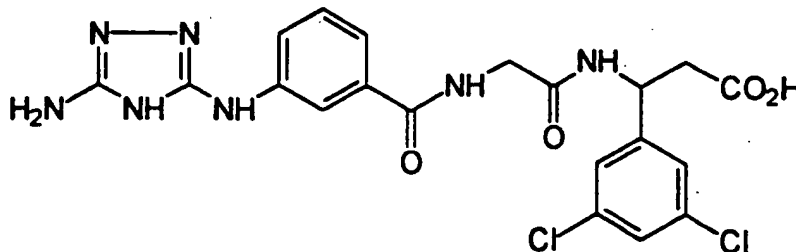
ethyl β -[[2-[[[3-[(benzoxazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate.

β -[[2-[[[3-[(5,6-dihydro-4H-thiazin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

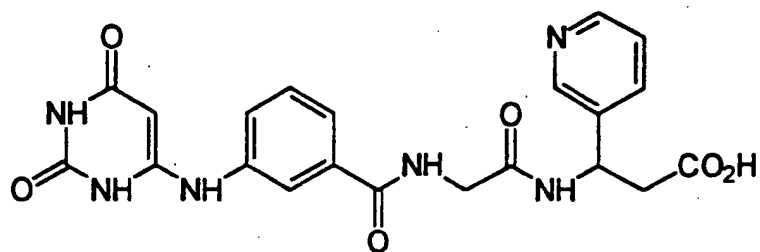
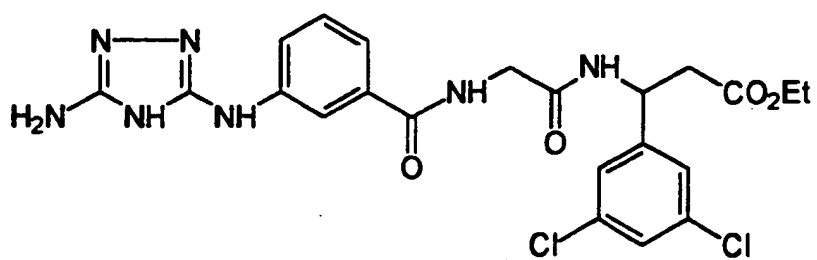
and

ethyl β -[[2-[[[3-[(5,6-dihydro-4H-thiazin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate.

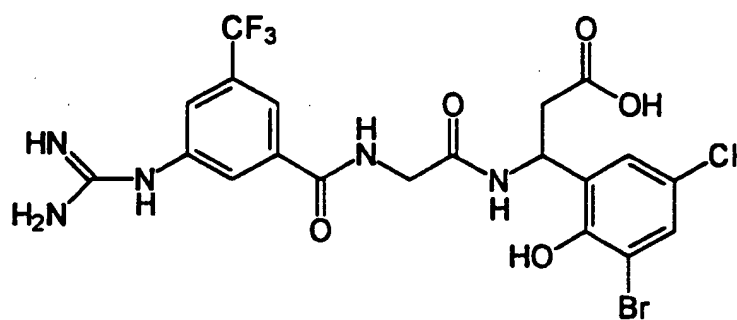
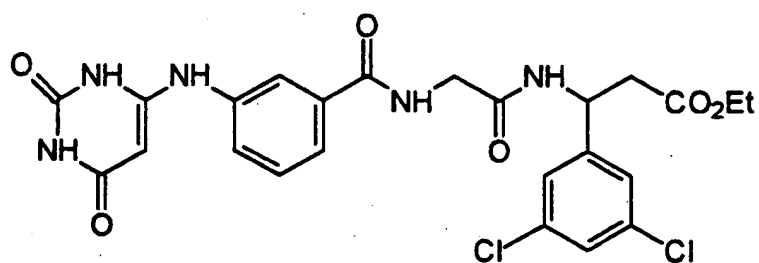
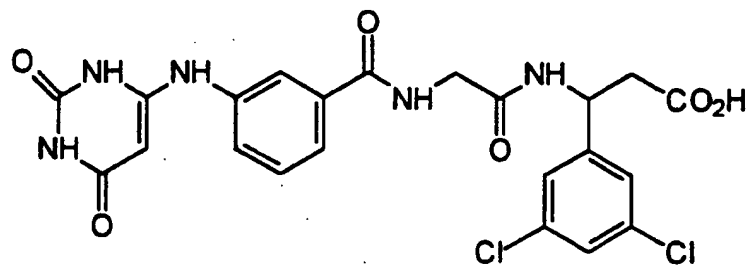
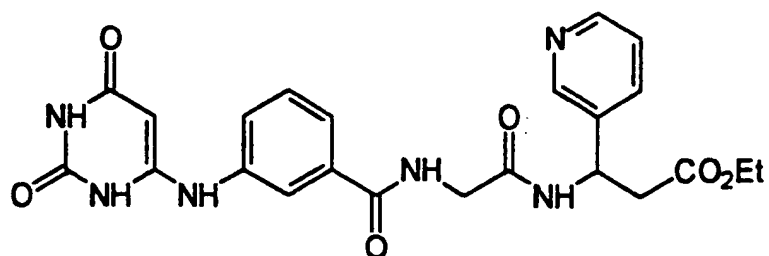
40. A pharmaceutical composition according to Claim 21 wherein the compound is selected from the group consisting of



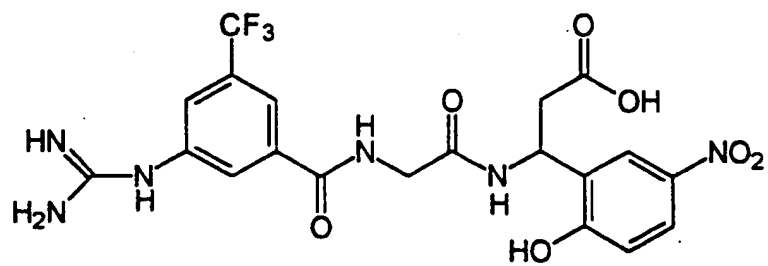
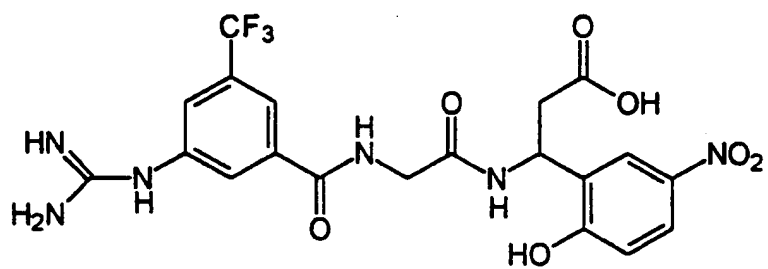
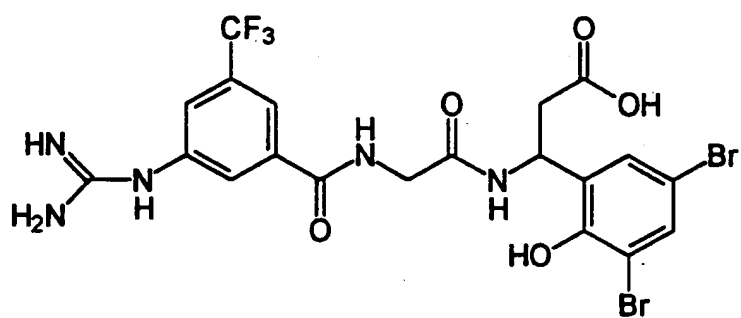
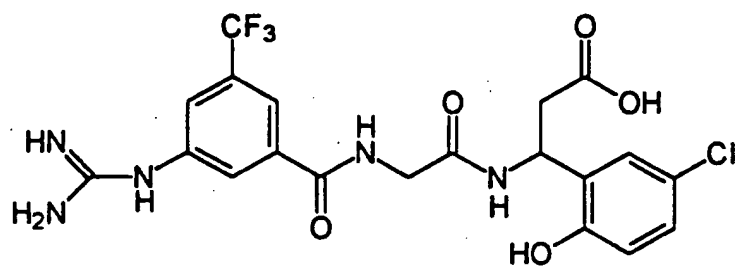
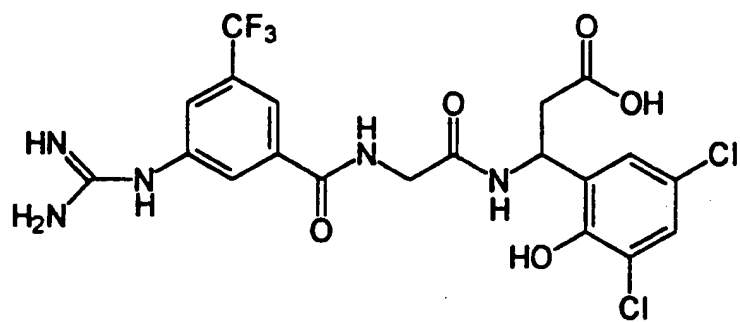
- 857 -



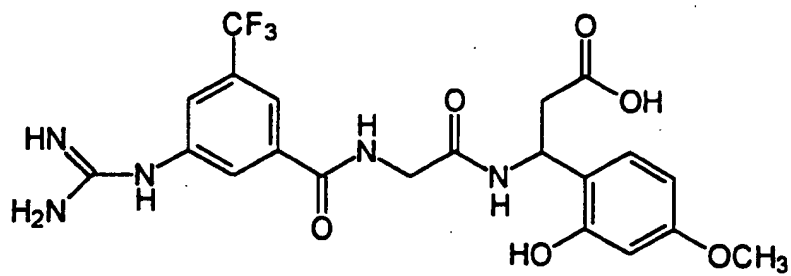
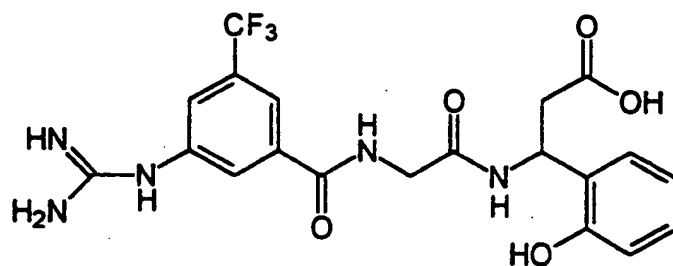
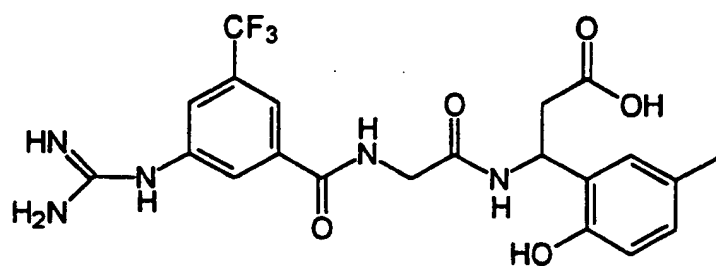
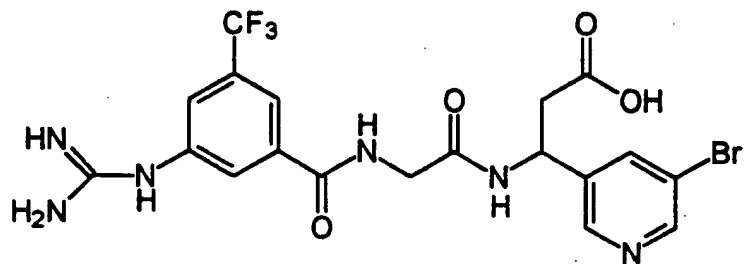
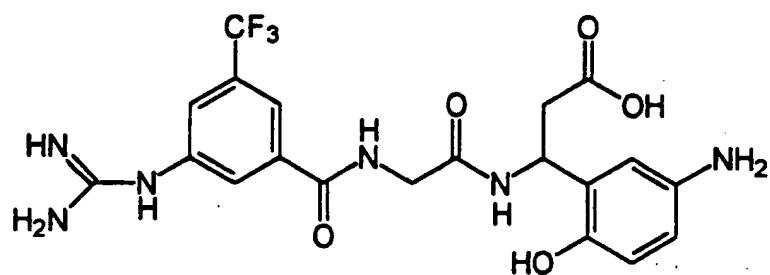
- 858 -



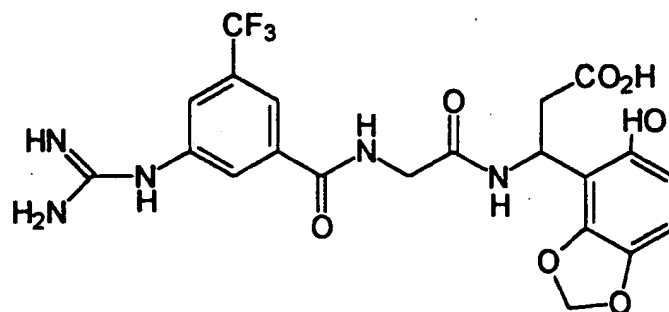
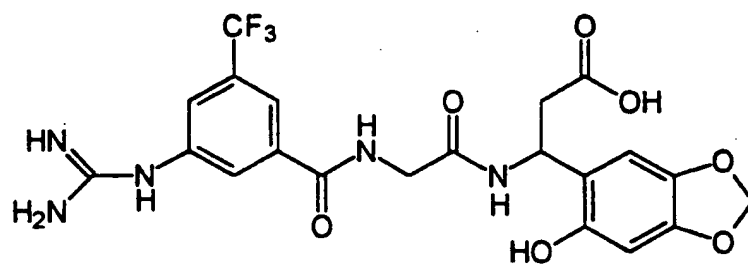
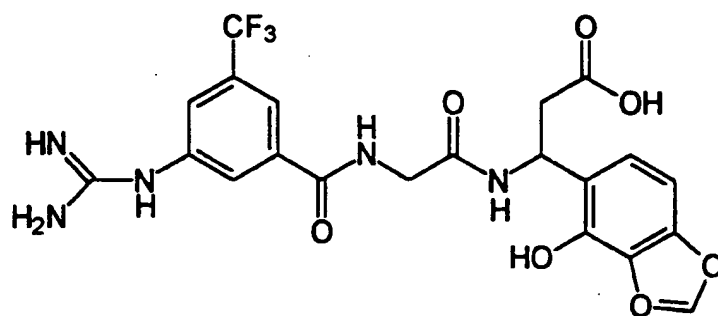
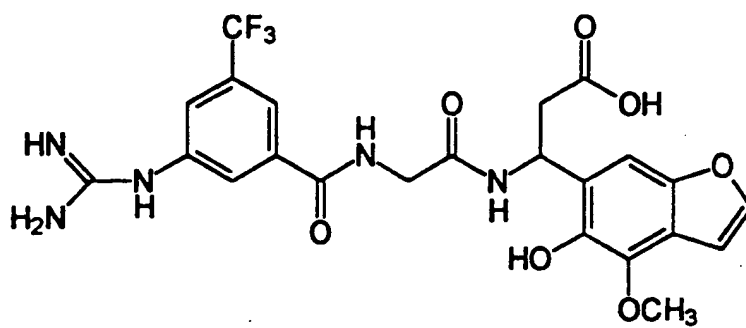
- 859 -



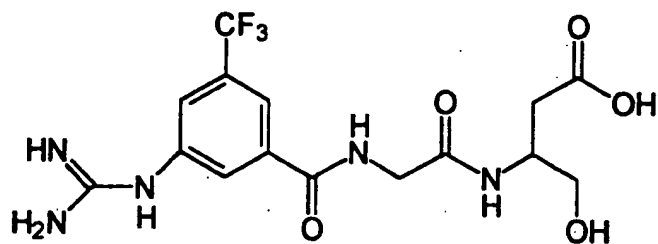
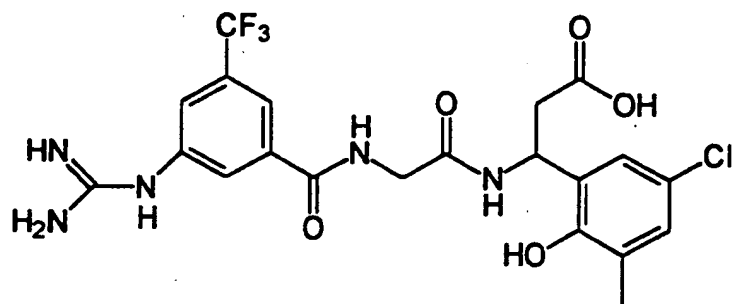
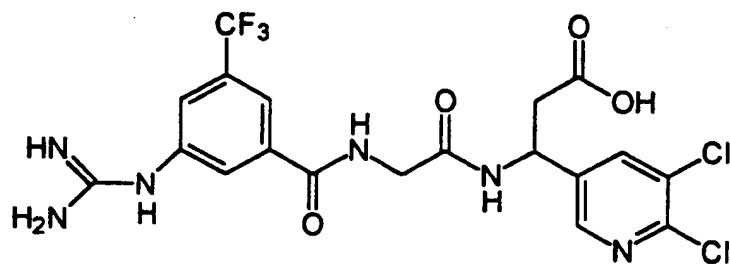
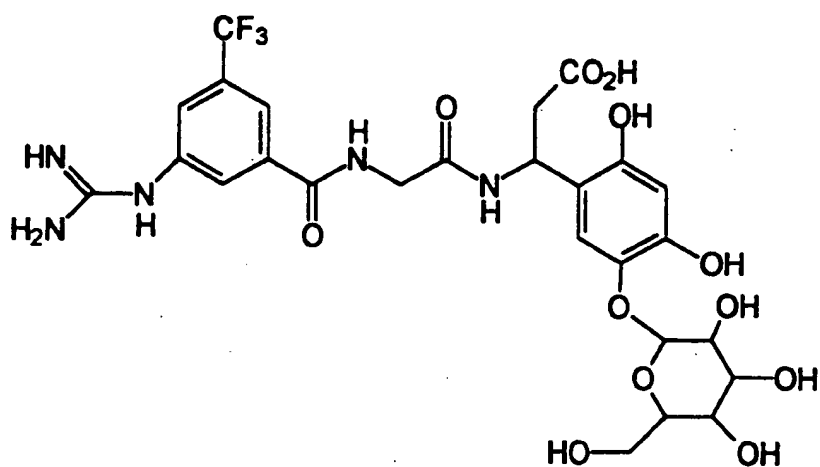
- 860 -



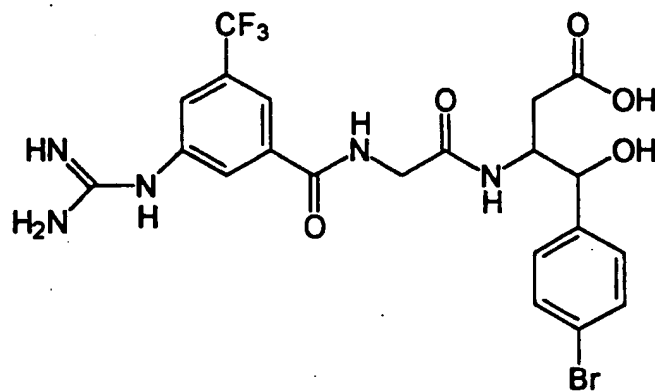
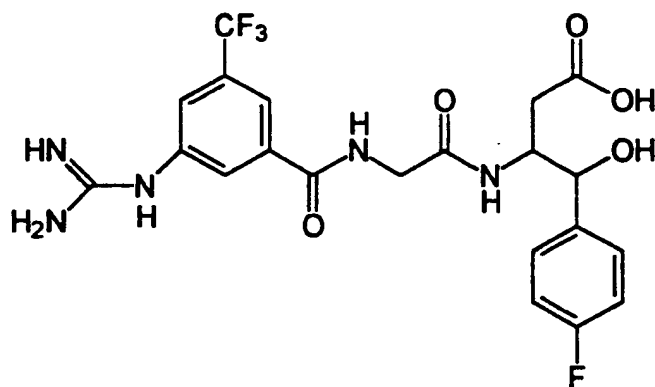
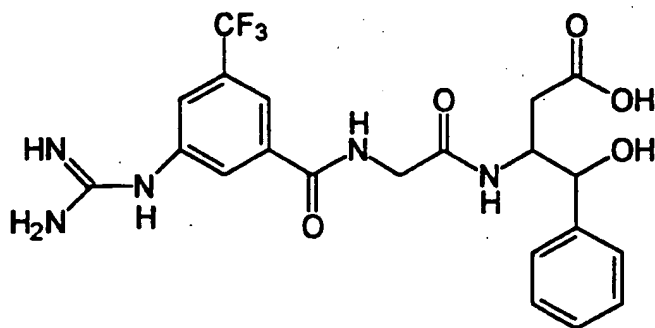
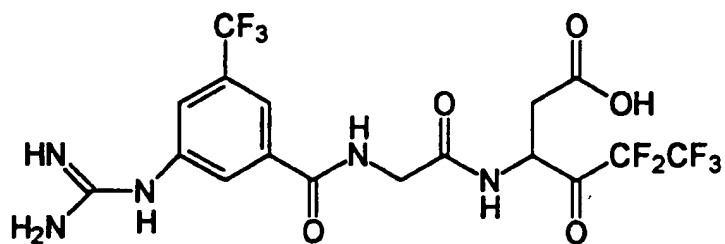
- 861 -



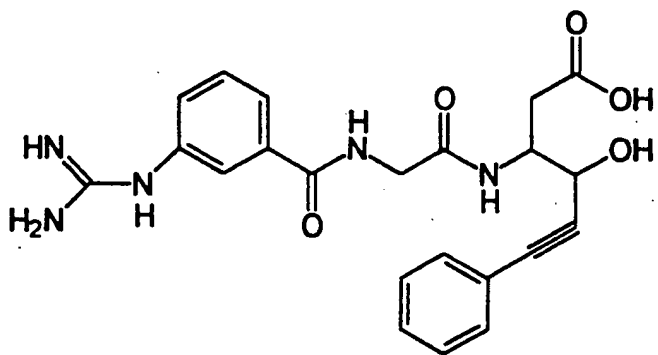
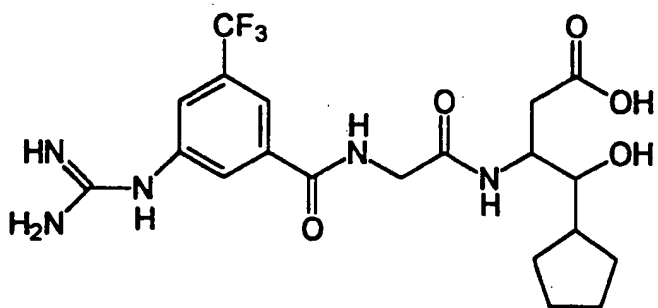
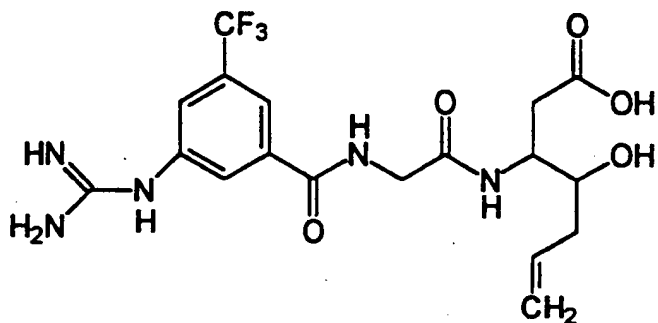
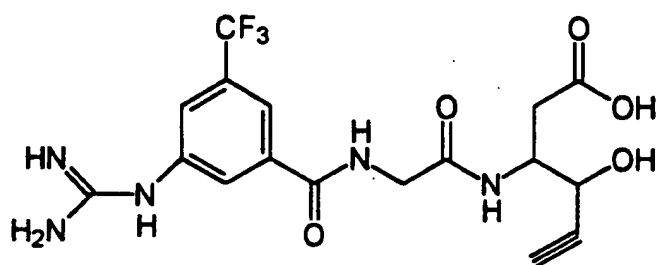
- 862 -



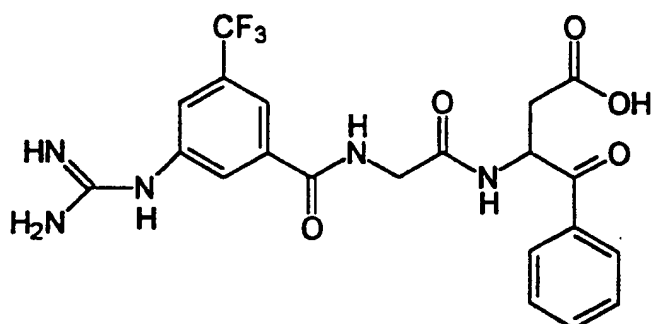
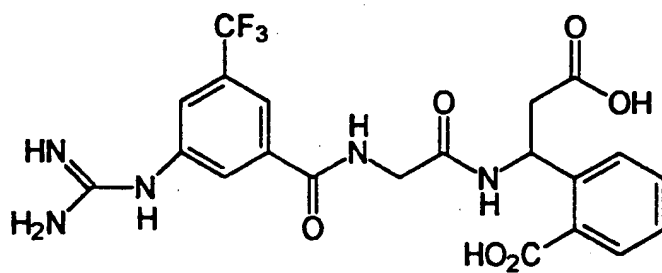
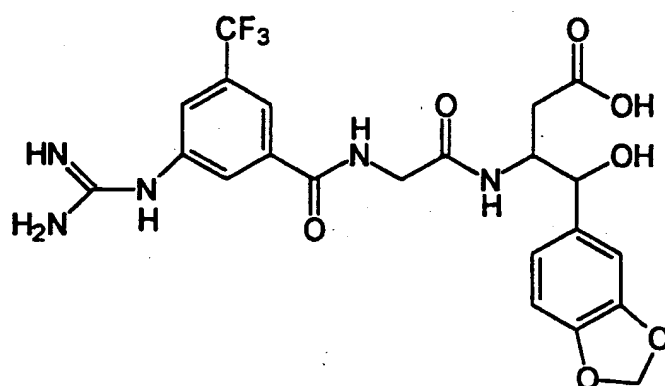
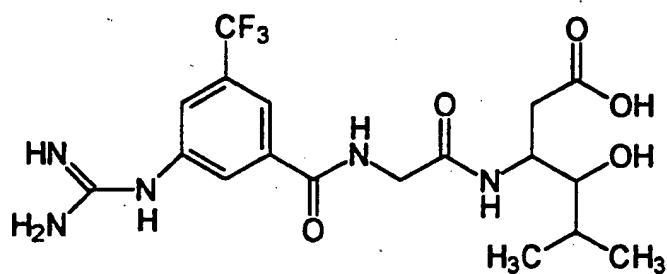
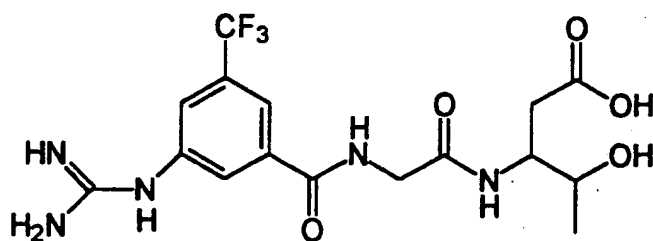
- 863 -



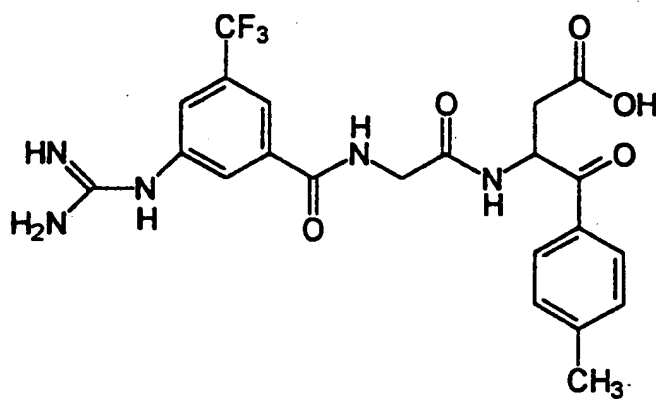
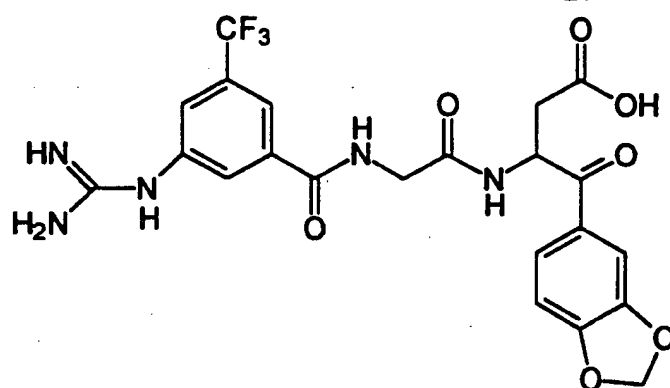
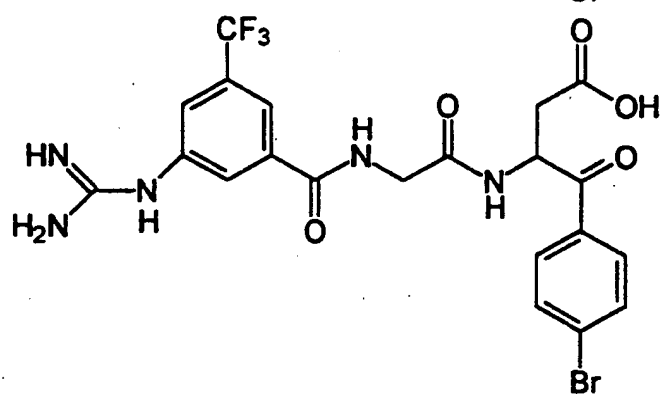
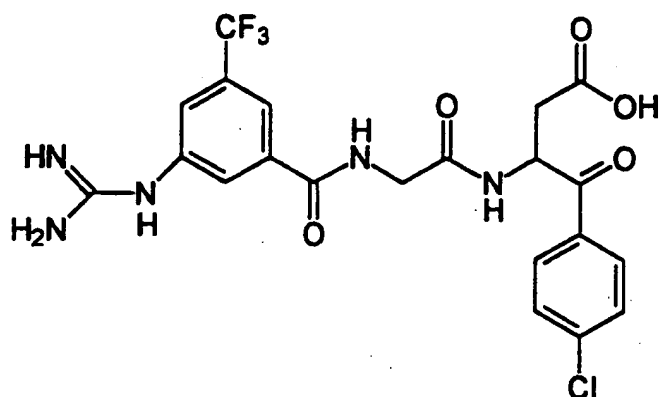
- 864 -



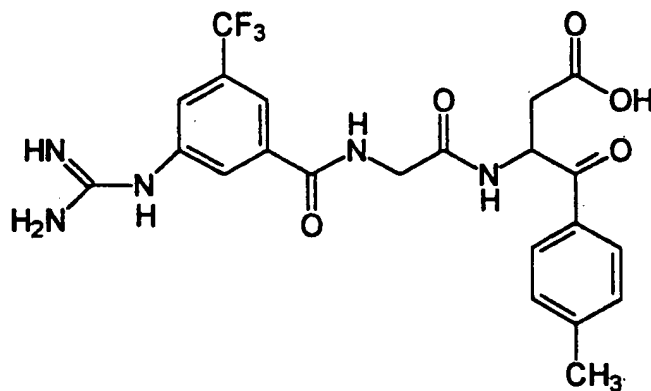
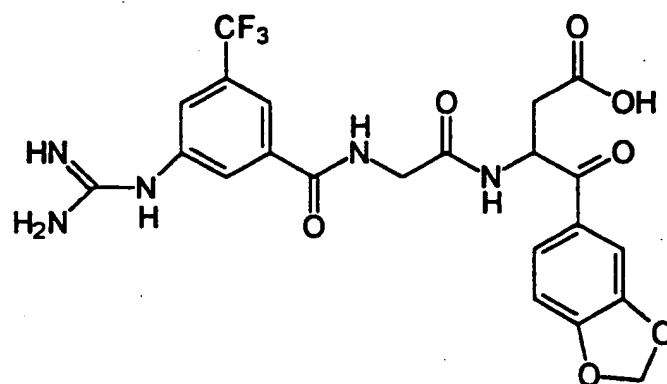
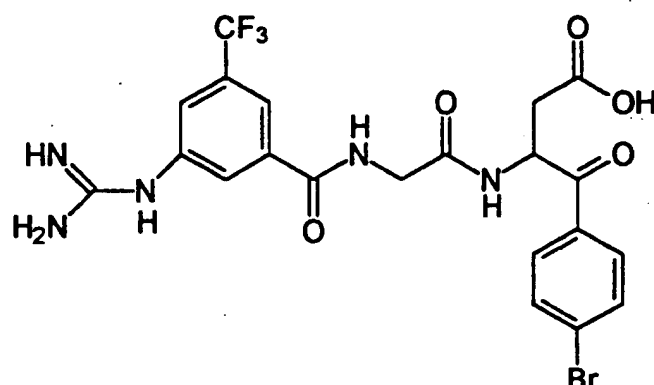
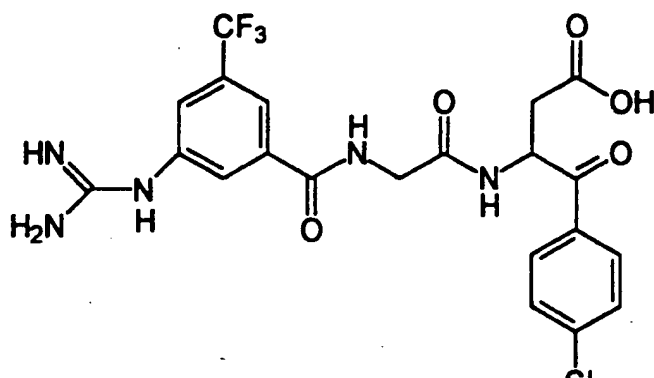
- 865 -



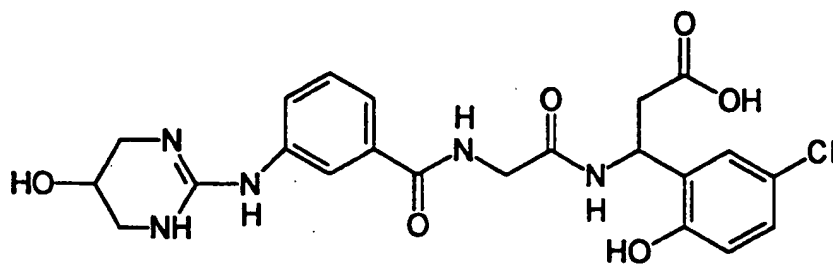
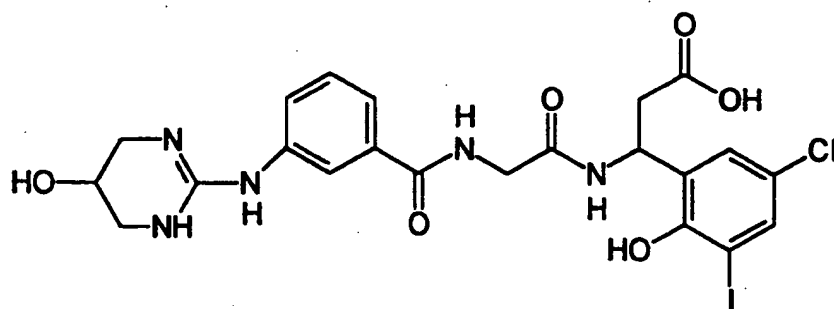
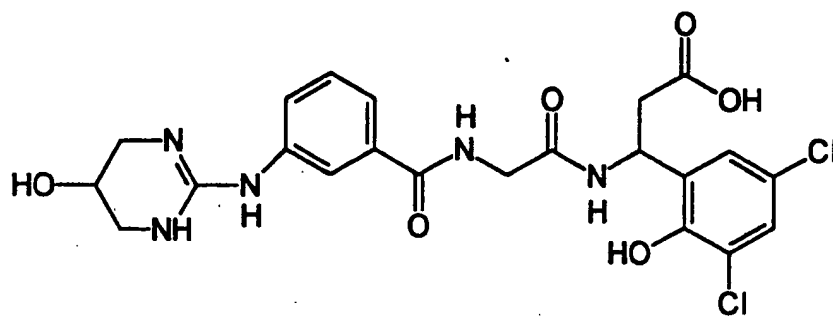
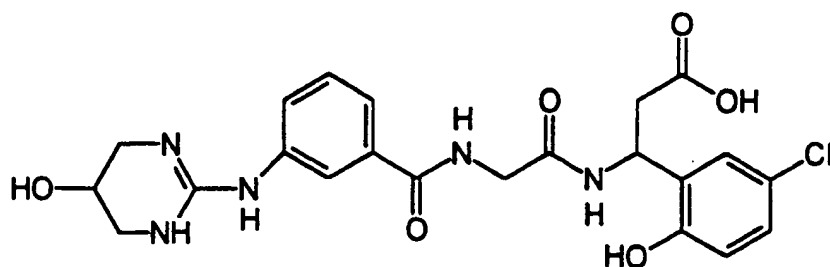
- 866 -



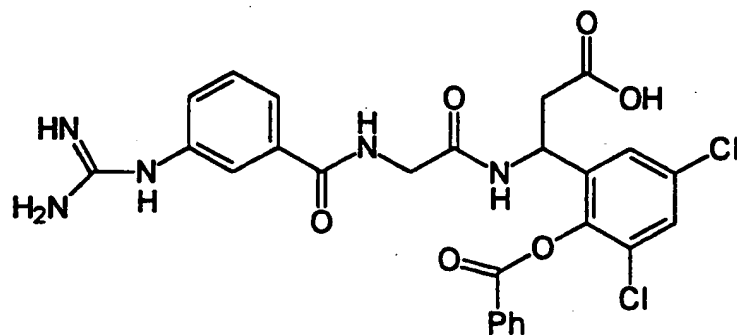
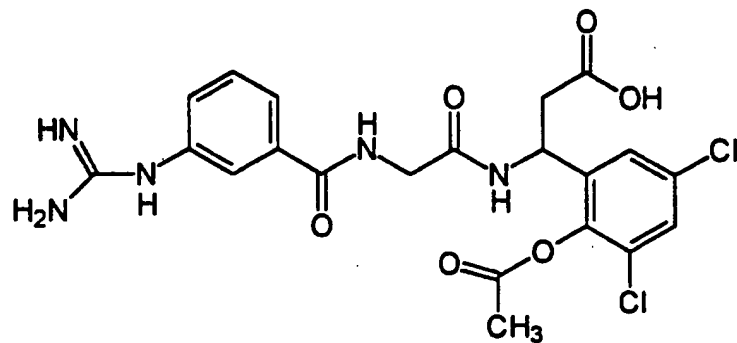
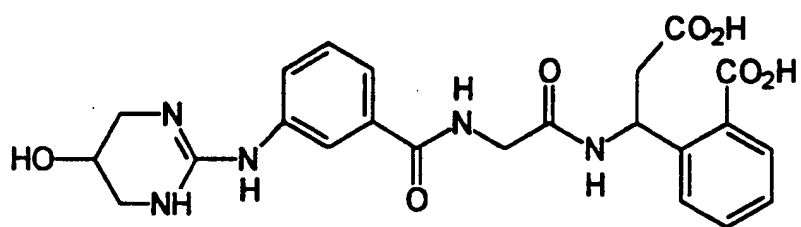
- 867 -



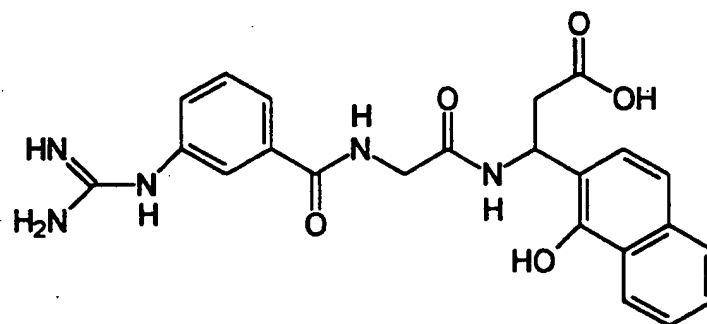
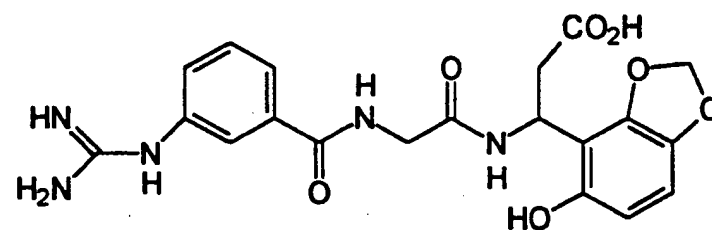
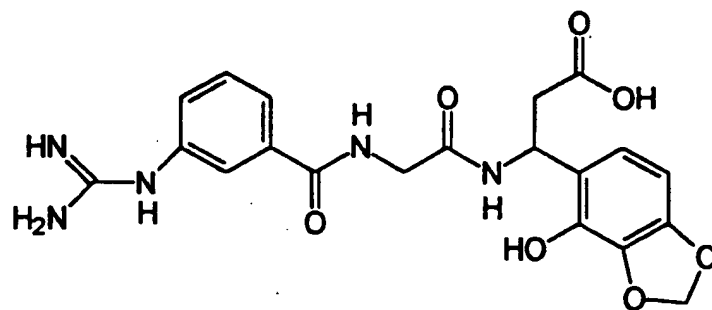
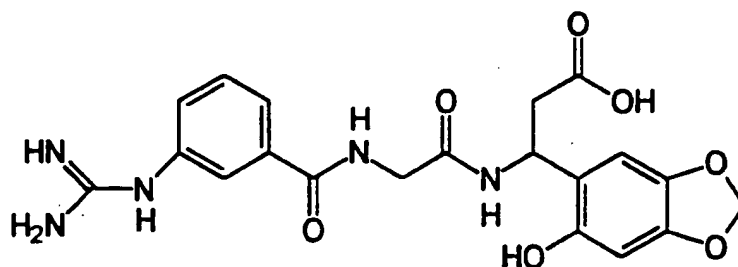
- 868 -



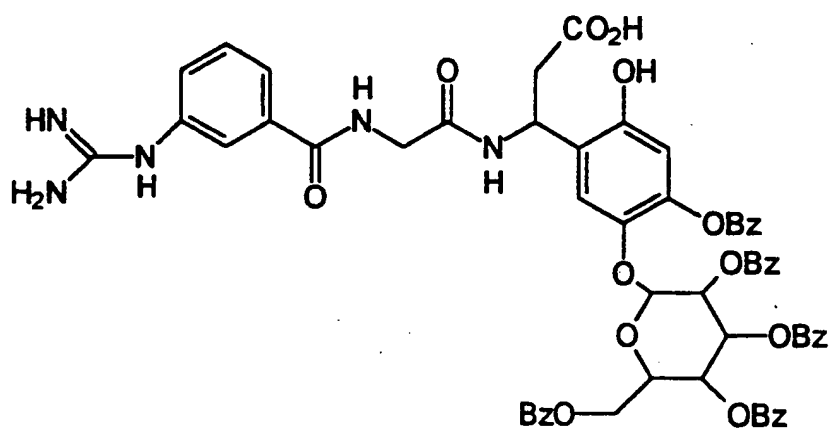
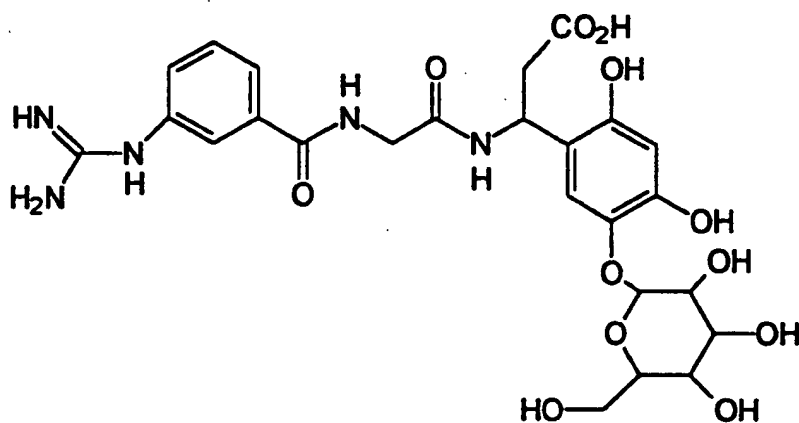
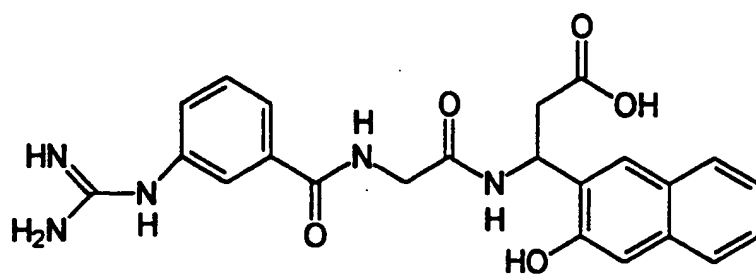
- 870 -



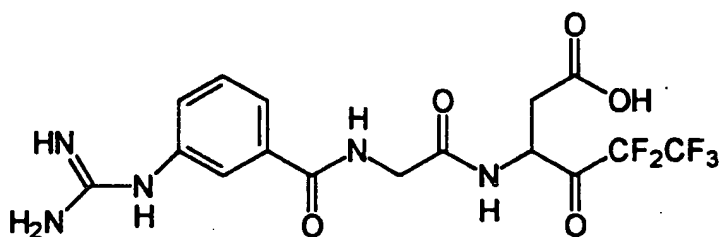
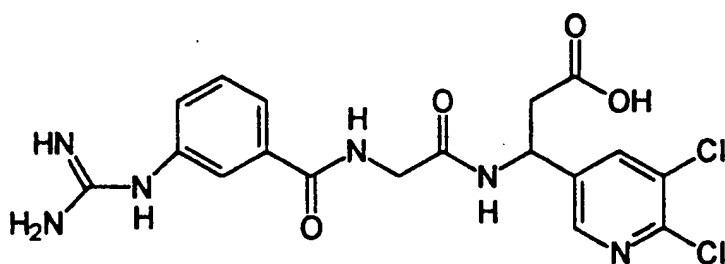
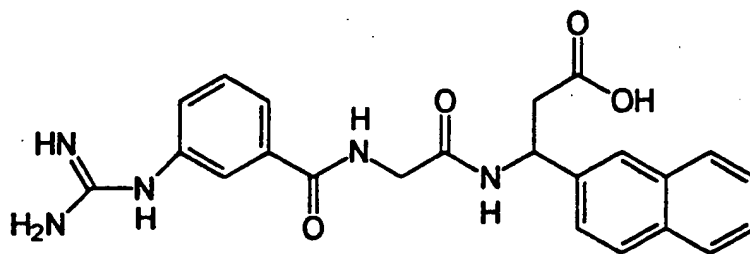
- 871 -



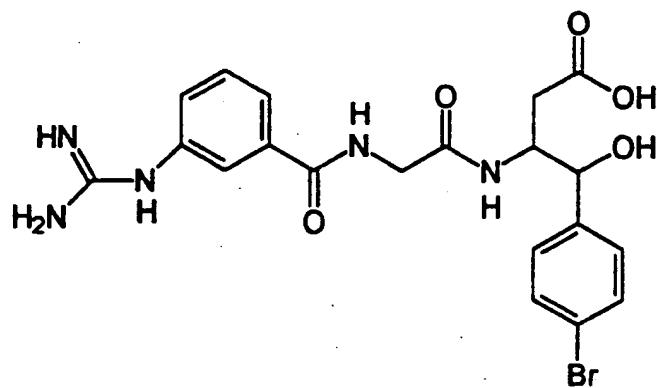
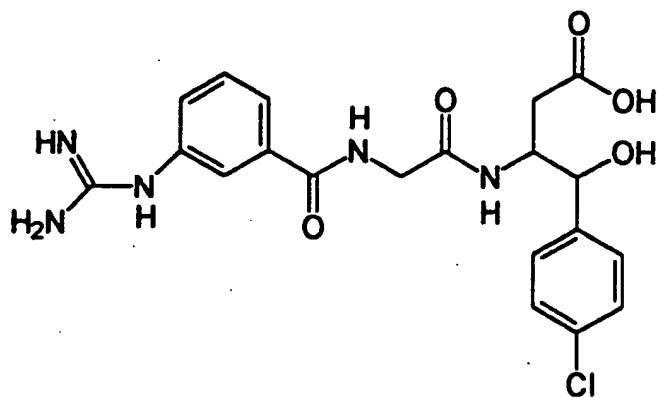
- 872 -



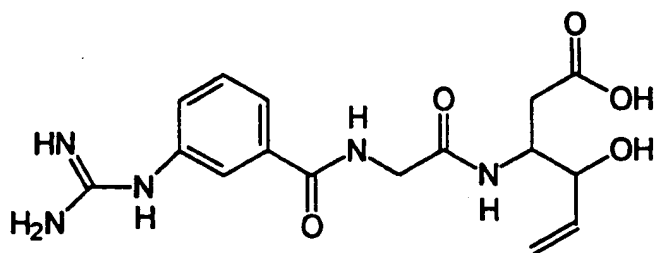
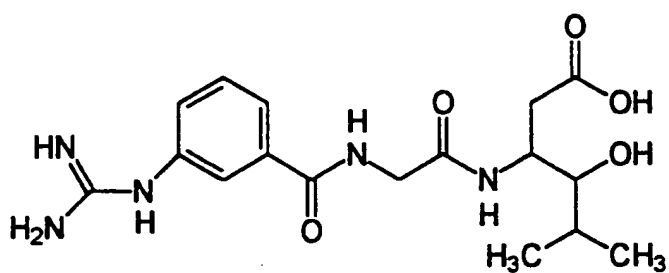
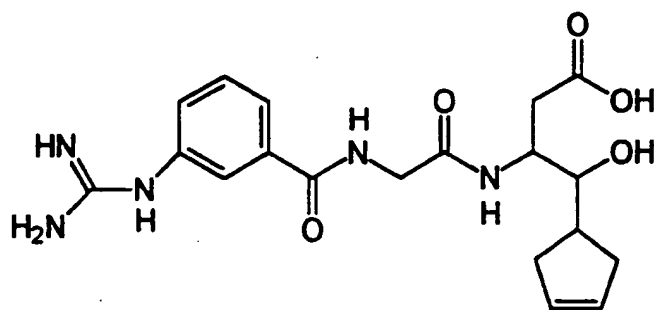
- 873 -



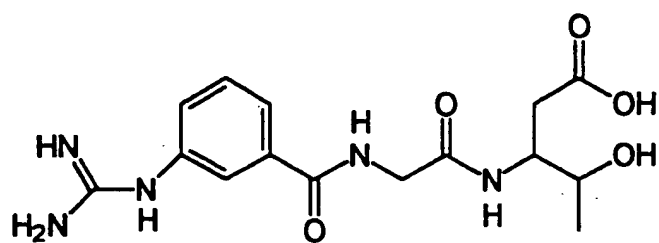
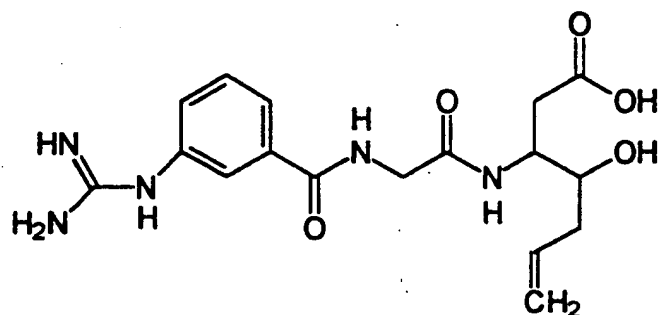
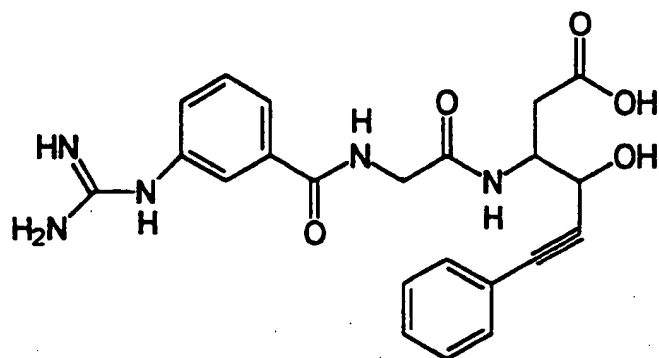
- 874 -



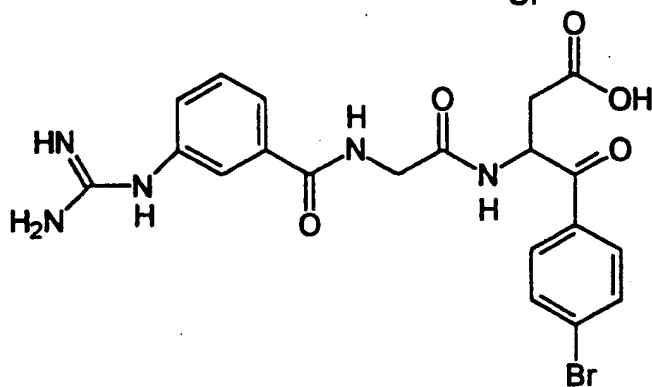
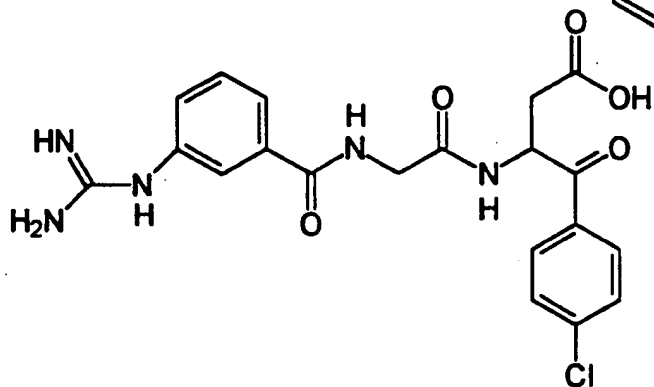
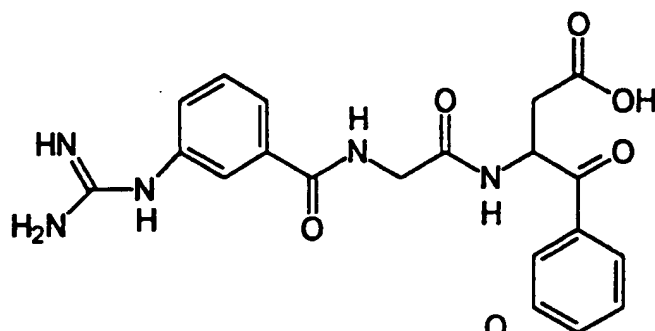
- 875 -



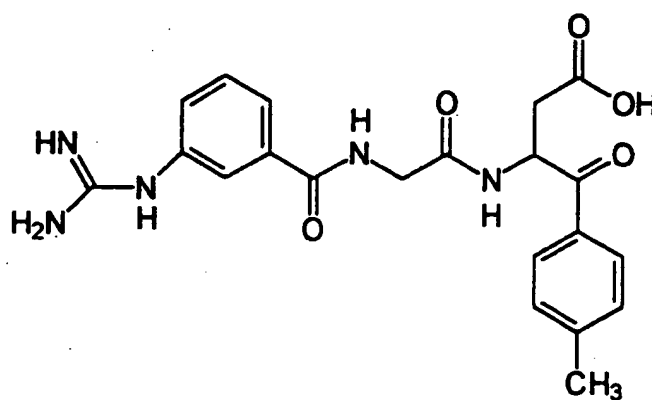
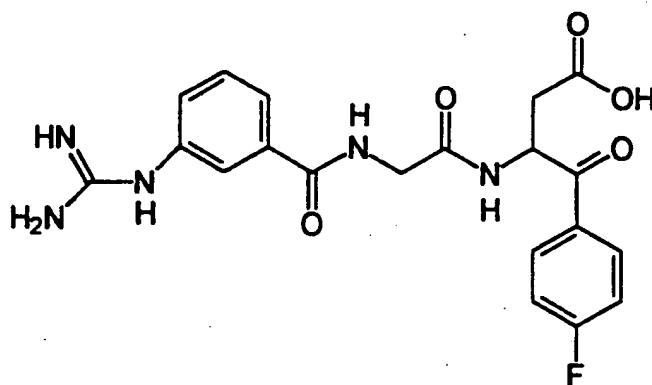
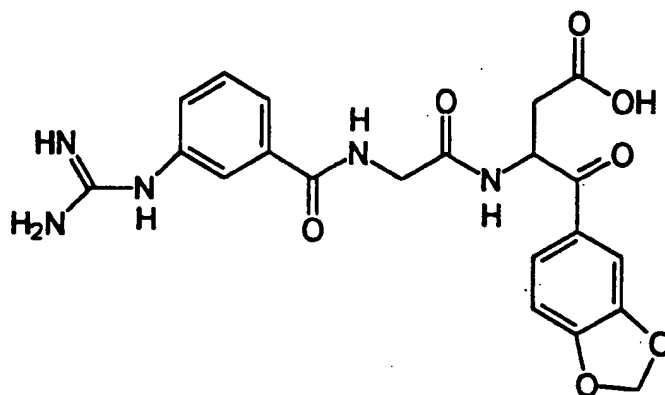
- 876 -



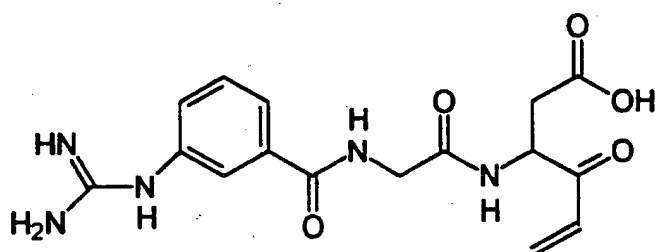
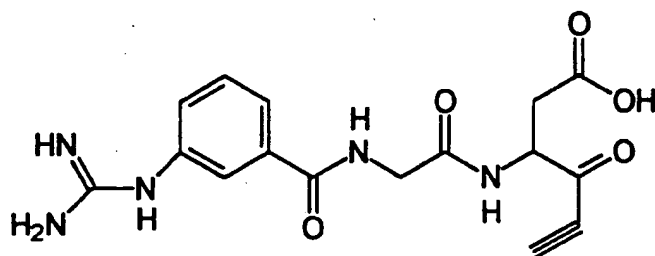
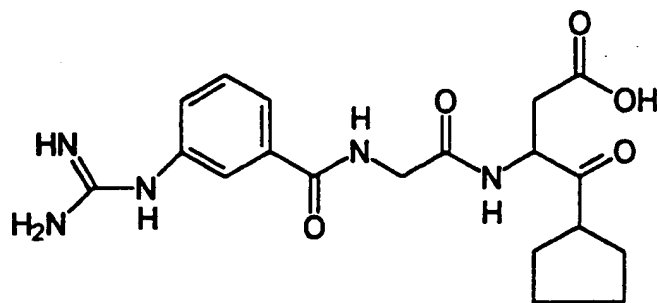
- 877 -



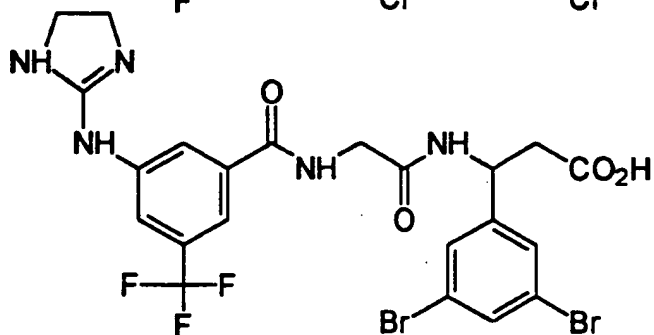
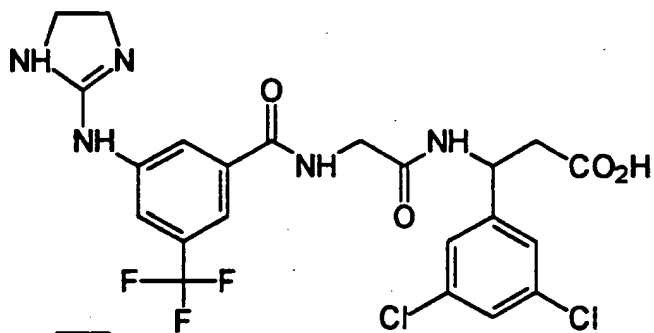
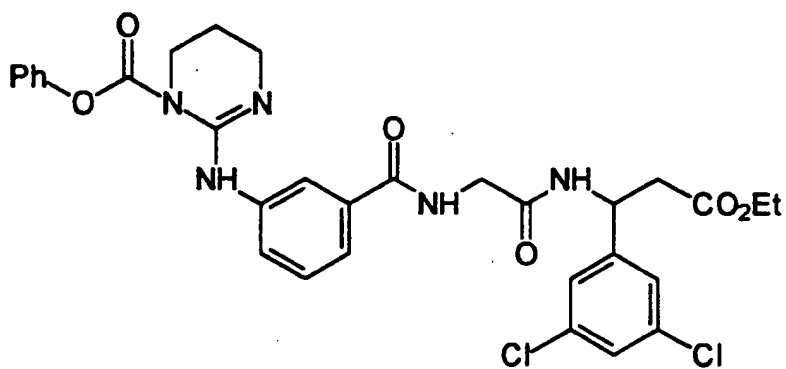
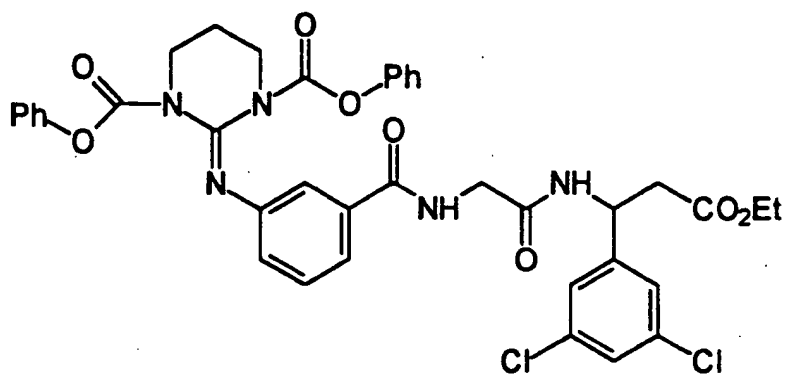
- 878 -



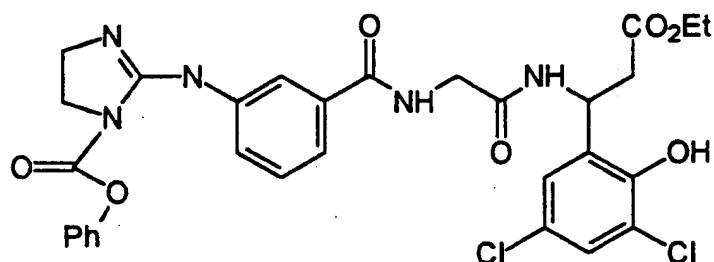
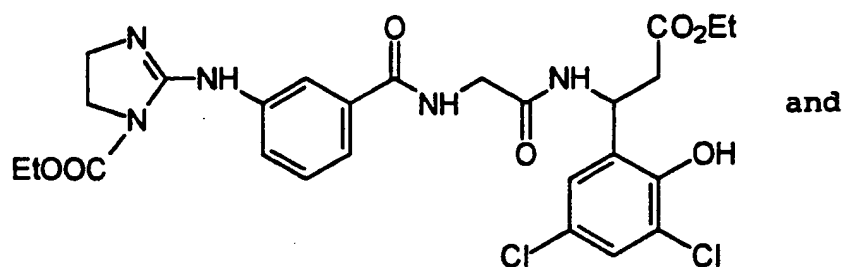
- 879 -



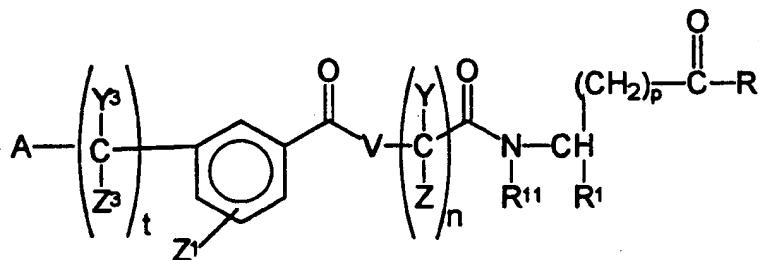
- 880 -



- 881 -

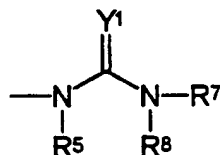


41. A method for treating conditions mediated by the $\alpha_v\beta_3$ integrin in a mammal in need of such treatment comprising administering an effective $\alpha_v\beta_3$ inhibiting amount of a compound of the formula



or a pharmaceutically acceptable salt thereof,
wherein

A is



- 882 -

wherein Y¹ is selected from the group consisting of N-R², O, and S;

R² is selected from the group consisting of H; alkyl; aryl; hydroxy; alkoxy; cyano; nitro; amino; alkenyl; alkynyl; amido; alkylcarbonyl; arylcarbonyl; alkoxycarbonyl; aryloxycarbonyl; haloalkylcarbonyl; haloalkoxycarbonyl; alkylthiocarbonyl; arylthiocarbonyl; acyloxymethoxycarbonyl; alkyl optionally substituted with one or more substituent selected from lower alkyl, halogen, hydroxyl, haloalkyl, cyano, nitro, carboxyl, amino, alkoxy, aryl or aryl optionally substituted with one or more halogen, haloalkyl, lower alkyl, alkoxy, cyano, alkylsulfonyl, alkylthio, nitro, carboxyl, amino, hydroxyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles, or fused monocyclic heterocycles; aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, hydroxy, lower alkyl, alkoxy, methylenedioxy, ethylenedioxy, cyano, nitro, alkylthio, alkylsulfonyl, sulfonic acid, sulfonamide, carboxyl derivatives, amino, aryl, fused aryl, monocyclic heterocycles and fused monocyclic heterocycle; monocyclic heterocycles; and monocyclic heterocycles optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, amino, nitro, hydroxy, carboxyl derivatives, cyano, alkylthio, alkylsulfonyl, sulfonic acid, sulfonamide, aryl or fused aryl; or

R² taken together with R⁷ forms a 4-12 membered dinitrogen containing heterocycle optionally substituted with one or more substituent selected from the group consisting of lower alkyl, hydroxy,

- 883 -

k to, alkoxy, halo, phenyl, amino, carboxyl or carboxyl ester, and fused phenyl;

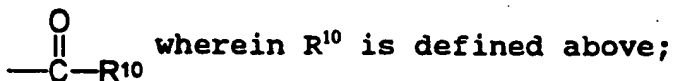
or R^2 taken together with R^7 forms a 5 membered heteroaromatic ring optionally substituted with one or more substituent selected from lower alkyl, phenyl and hydroxy;

or R^2 taken together with R^7 forms a 5 membered heteroaromatic ring fused with a phenyl group;

R^7 (when not taken together with R^2) and R^8 are independently selected from the group consisting of H; alkyl; alkenyl; alkynyl; aralkyl; amino; alkylamino; hydroxy; alkoxy; arylamino; amido, alkylcarbonyl, arylcarbonyl; alkoxycarbonyl; aryloxy; haloalkylcarbonyl; aryloxy; haloalkoxycarbonyl; alkylthiocarbonyl; arylthiocarbonyl; acyloxymethoxycarbonyl; cycloalkyl; bicycloalkyl; aryl; acyl; benzoyl; alkyl optionally substituted with one or more substituent selected from lower alkyl, halogen, hydroxy, haloalkyl, cyano, nitro, carboxyl derivatives, amino, alkoxy, thio, alkylthio, sulfonyl, aryl, aralkyl, aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, carboxyl derivatives, aryloxy, amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethyl, sulfonyl, alkylsulfonyl, haloalkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles, fused monocyclic heterocycles; aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy,

- 884 -

methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, carboxyl derivatives, aryloxy, amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethylsulfonyl, alkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles, or fused monocyclic heterocycles; monocyclic heterocycles; monocyclic heterocycles optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, aryloxy, amino, nitro, hydroxy, carboxyl derivatives, cyano, alkylthio, alkylsulfonyl, aryl, fused aryl; monocyclic and bicyclic heterocyclicalkyls; $-SO_2R^{10}$ wherein R^{10} is selected from the group consisting of alkyl, aryl and monocyclic heterocycles, all optionally substituted with one or more substituent selected from the group consisting of halogen, haloalkyl, alkyl, alkoxy, cyano, nitro, amino, acylamino, trifluoroalkyl, amido, alkylaminosulfonyl, alkylsulfonyl, alkylsulfonylamino, alkylamino, dialkylamino, trifluoromethylthio, trifluoroalkoxy, trifluoromethylsulfonyl, aryl, aryloxy, thio, alkylthio, and monocyclic heterocycles; and

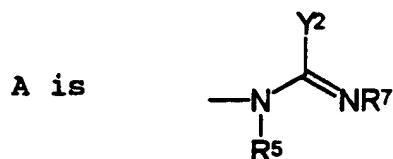


or NR^7 and R^8 taken together form a 4-12 membered mononitrogen containing monocyclic or bicyclic ring optionally substituted with one or more substituent selected from lower alkyl, carboxyl derivatives, aryl or hydroxy and wherein said ring optionally contains a heteroatom selected from the group consisting of O, N and S;

- 885 -

R^5 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, benzyl, and phenethyl;

or



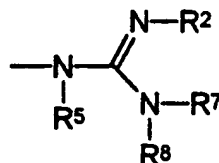
wherein Y^2 is selected from the group consisting of alkyl; cycloalkyl; bicycloalkyl; aryl; monocyclic heterocycles; alkyl optionally substituted with aryl which can also be optionally substituted with one or more substituent selected from halo, haloalkyl, alkyl, nitro, hydroxy, alkoxy, aryloxy, aryl, or fused aryl; aryl optionally substituted with one or more substituent selected from halo, haloalkyl, hydroxy, alkoxy, aryloxy, aryl, fused aryl, nitro, methylenedioxy, ethylenedioxy, or alkyl; alkynyl; alkenyl; $-S-R^9$ and $-O-R^9$ wherein R^9 is selected from the group consisting of H; alkyl; aralkyl; aryl; alkenyl; and alkynyl; or R^9 taken together with R^7 forms a 4-12 membered mononitrogen and monosulfur or monooxygen containing heterocyclic ring optionally substituted with lower alkyl, hydroxy, keto, phenyl, carboxyl or carboxyl ester, and fused phenyl; or R^9 taken together with R^7 is thiazole; oxazole; benzoxazole; or benzothiazole; and

R^5 and R^7 are as defined above;

or Y^2 (when Y^2 is carbon) taken together with R^7 forms a 4-12 membered mononitrogen containing ring optionally substituted with alkyl, aryl or hydroxy;

- 886 -

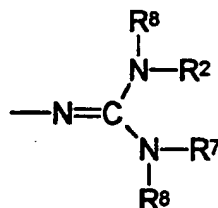
or A is



where R^2 and R^7 taken together form a 5-8 membered dinitrogen containing heterocycle optionally substituted with one or more substituent selected from the group consisting of lower alkyl, hydroxy, keto, phenyl, or carboxyl derivatives; and R^8 is selected from the group consisting of alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkylcarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl, or acyloxymethoxycarbonyl; and

R^5 is defined as above

or A is



where R^2 and R^7 taken together form a 5-8 membered dinitrogen containing heterocycle optionally substituted with hydroxy, keto, phenyl, or alkyl; and

R^8 are both selected from the group consisting of alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkylcarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl and acyloxymethoxycarbonyl;

- 887 -

Z¹ is one or more substituent selected from the group consisting of H; alkyl; hydroxy; alkoxy; aryloxy; halogen; haloalkyl; haloalkoxy; nitro; amino; alkylamino; acylamino; dialkylamino; cyano; alkylthio; alkylsulfonyl; carboxyl derivatives; trihaloacetamide; acetamide; aryl; fused aryl; cycloalkyl; thio; monocyclic heterocycles; fused monocyclic heterocycles; and A, wherein A is defined above;

V is selected from the group consisting of -N-(R⁶)- wherein R⁶ is selected from the group consisting of H; lower alkyl; cycloalkyl; aralkyl; aryl; and monocyclic heterocycles; or R⁶ taken together with Y, forms a 4-12 membered mononitrogen containing ring;

Y, Y³, Z and Z³ are independently selected from the group consisting of hydrogen; alkyl; aryl; and cycloalkyl; or Y and Z taken together form a cycloalkyl; or Y³ and Z³ taken together form a cycloalkyl;

n is an integer 1, 2, or 3;

t is an integer 0, 1, or 2;

p is an integer 0, 1, 2, or 3;

R is X-R³ wherein X is selected from the group consisting of O, S and NR⁴, wherein R³ and R⁴ are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; haloalkyl; aryl; arylalkyl; sugars; steroids; polyalkylethers; alkylamido; alkyl N,N-dialkylamido; pivaloyloxymethyl; and in the case

- 888 -

of the free acid, all pharmaceutically acceptable salts thereof;

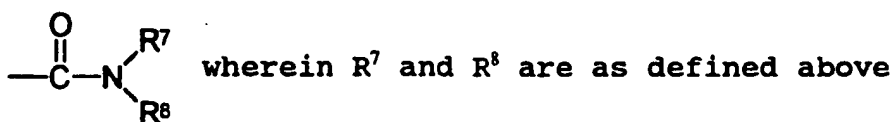
R¹ is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; carboxyl derivatives; haloalkyl; monocyclic heterocycles; monocyclic heterocycles optionally substituted with alkyl, halogen, haloalkyl, cyano, hydroxy, aryl, fused aryl, nitro, alkoxy, aryloxy, alkylsulfonyl, arylsulfonyl, sulfonamide, thio, alkylthio, carboxyl derivatives, amino, amido;

alkyl optionally substituted with one or more of halo, haloalkyl, hydroxy, alkoxy, aryloxy, thio, alkylthio, alkynyl, alkenyl, alkyl, arylthio, alkylsulfoxide, alkylsulfonyl, arylsulfoxide, arylsulfonyl, cyano, nitro, amino, alkylamino, dialkylamino, alkylsulfonamide, arylsulfonamide, acylamide, carboxyl derivatives, sulfonamide, sulfonic acid, phosphonic acid derivatives, phosphinic acid derivatives, aryl, arylthio, arylsulfoxide, or arylsulfone all optionally substituted on the aryl ring with halo, alkyl, haloalkyl, cyano, nitro, hydroxy, carboxyl derivatives, alkoxy, aryloxy, amino, alkylamino, dialkylamino, amido, aryl, fused aryl, monocyclic heterocycles; and fused monocyclic heterocycles, monocyclic heterocyclicthio, monocyclic heterocyclicsulfoxide, and monocyclic heterocyclic sulfone, which can be optionally substituted with halo, haloalkyl, nitro, hydroxy, alkoxy, fused aryl, or alkyl;

alkylcarbonyl, haloalkylcarbonyl, and arylcarbonyl;

- 889 -

aryl optionally substituted in one or more positions with halo, haloalkyl, alkyl, alkoxy, aryloxy, methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, acyloxy, carboxyl derivatives, carboxyalkoxy, amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethylsulfonyl, alkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles and fused monocyclic heterocycles; and



and provided that taken together with the nitrogen, R⁷ and R⁸ comprise an amino acid;

and

R¹¹ is selected from the group consisting of H, alkyl, aralkyl, alkenyl, alkynyl, haloalkyl or haloalkynyl or R¹¹ taken together with Y forms a 4-12 membered mononitrogen containing ring.

42. A method according to claim 41 wherein the compound is selected from

(±)ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]pyridine-3-propanoate;

(±)β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid;

(±)ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]benzenepropanoate;

- 890 -

(±)β-[[2-[[[3-
[(aminoiminomethyl)amino]phenyl]carbonyl]-
amino]acetyl]amino]benzenepropanoic acid;

(±)ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-1,3-
benzodioxole-5-propanoate;

(±)β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-1,3-
benzodioxole-5-propanoic acid;

(±)ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]-
naphthalen-1-yl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoate;

(±)β-[[2-[[[3-[(aminoiminomethyl)-amino]-
naphthalen-1-yl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

(±)ethyl β-[[1-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]-1-cyclopropyl]-
carbonyl]amino]pyridine-3-propanoate;

(±)β-[[1-[[[3[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]cycloprop-1-yl]carbonyl]-
amino]pyridine-3-propanoic acid;

(±)ethyl β-[[2-[[[3-[[imino[(phenylmethyl)amino]-
methyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoate;

- 891 -

(±) β -[[2-[[[3-[[imino[(ph nylmethyl)amino)methyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

3S-[[2-[[[3-(aminocarbonylamino)phenyl]-carbonyl]amino]acetyl]amino]-4-pentynoic acid;

ethyl 3S-[[2-[[[3-(aminocarbonylamino)phenyl]-carbonyl]amino]acetyl]amino]-4-pentynoate;

β S-[[2-[[[3-[(aminoiminomethyl)amino]-2,5,6-trifluorophenyl]carbonyl]amino]acetyl]-amino]-4-pentynoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

ethyl (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-[1,1'-biphenyl]-4-propanoic acid;

thyl (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-[1,1'-biphenyl]-4-propanoate;

- 892 -

(±) ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)-phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid ;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-naphthalene-1-carboxylic acid;

methyl (±) β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-naphthalene-1-carboxylate;

(±) 3-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]-2-oxopyrrolidine-1-propanoic acid;

3R-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-4-pentynoic acid;

ethyl 3R-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-4-pentynoate;

3S-[[2-[[[3-[[[(phenylmethyl)amino]-carbonyl]amino]phenyl]carbonyl]amino]acetyl]-amino]-4-pentynoic acid;

ethyl 3S-[[2-[[[3-[[[(phenylmethyl)amino]-carbonyl]amino]phenyl]carbonyl]amino]acetyl]-amino]-4-pentynoate;

3S-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-4-pentynoic acid;

- 893 -

β -[[2-[[[3-(aminocarbonylamino)phenyl]-
carbonyl]amino]acetyl]amino]pyridine-
3-propanoic acid;

ethyl β -[[2-[[[3-(aminocarbonylamino)phenyl]-
carbonyl]amino]acetyl]amino]pyridine-3-propanoate;

(\pm) β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

(\pm) ethyl β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoate;

(\pm) ethyl β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]-
amino]furan-2-propanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
furan-3-propanoic acid;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]-
amino]acetyl]amino]pentanedioic acid;

bismethyl ester 3-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]-amino]acetyl]amino]pentanedioate;

(\pm) hydrogen methyl 3-[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pentanedioate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
furan-2-propanoic acid;

- 894 -

ethyl (±) β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]furan-2-propanoate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
naphthalene-2-propanoic acid;

(±) methyl β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
thiophene-3-propanoate;

ethyl 3S-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
4-pentynoate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
thiophene-3-propanoic acid;

(±) 2-[3-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-4-
carboxybutyl]thio]benzoic acid;

(±) 2-[3-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-4-
carboxybutyl]sulfonyl]benzoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
thiophene-2-propanoic acid;

(±) methyl 2-[[3-[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-4-
carboxybutyl]thio]benzoate;

- 895 -

(±) methyl 3-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-5-[(4-methylphenyl)thio]pentanoate;

(±) methyl 3-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-4-[[[(4-methylphenyl)sulfonyl]amino]butanoate;

3-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-[[[(4-methylphenyl)sulfonyl]amino]butanoic acid;

(±) 3-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-5-[(4-methylphenyl)thio]pentanoic acid;

(±) 3-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-5-[(4-methylphenyl)sulfonyl]pentanoic acid;

3S-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-4-(phenylthio)butanoic acid;

3R-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-pentynoic acid;

ethyl 3R-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-pentynoate;

2-[[2S-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-2-(carboxymethyl)ethyl]sulfonyl]benzoic acid;

- 896 -

3S-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
4-pentynoic acid;

ethyl 3S-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
4-pentynoate;

2-[[2S-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-2-
(carboxymethyl)ethyl]thio]benzoic acid;

(±)ethyl β-[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]methylamino]acetyl]-
amino]-pyridine-3-propanoate;

(±)β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]methylamino]acetyl]amino]pyridine-
3-propanoic acid;

(±)ethyl β-[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]-1-oxopropyl]-
amino]pyridine-3-propanoate;

(±)β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]-1-oxopropyl]-
amino]pyridine-3-propanoic acid;

(±)β-[[2-[[[3-[(aminoiminomethyl)amino]-4-
methylphenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

(±)β-[[2-[[[3-[[[3-[(aminoiminomethyl)amino]-
methyl]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

- 897 -

3S-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
4-hydroxybutanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]-
amino]-2-hydroxybenzenepropanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-2-
hydroxy-5-methylbenzenepropanoic acid;

(±) 3-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-4-[(2-
hydroxyethyl)amino]-4-oxobutanoic acid;

2S-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3-
carboxypropyl 2-aminobenzoate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-1,4-
benzodioxin-6-propanoic acid;

N-[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]-β-alanine, ethyl ester;

N-[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]-β-alanine;

(±) ethyl β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
quinoline-3-propanoate;

β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
quinoline-3-propanoic acid;

- 898 -

N-[2-[[[3-[[[(ph nylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
 β -alanine, ethyl ester;

3-[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]
amino]propanoic acid;

(\pm)ethyl β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]
acetyl]amino]pyridine-3-propanoate;

(\pm) β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(phenylamino)carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate;

β -[[2-[[[3-[[[(phenylamino)carbonyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-(aminocarbonylamino)-
phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate;

β -[[2-[[[3-(aminocarbonylamino)phenyl]-
carbonyl]amino]acetyl]amino]pyridine-3-
propanoic acid;

ethyl β -[[2-[[[3-[[[(4-methylphenyl)sulfonyl]-
amino]carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]pyridine-3-propanoate;

- 899 -

β -[[2-[[[3-[[[(4-methylphenyl)sulfonyl]amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(aminothioxomethyl)-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoate;

β -[[2-[[[3-[(aminothioxomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]pyridine-
3-propanoic acid;

ethyl β -[[2-[[[3-[(aminothioxomethyl)amino]-
phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoate;

β -[[2-[[[3-[(aminothioxomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoic acid;

ethyl β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoate;

β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoic acid;

ethyl β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]-1,3-benzodioxole-5-propanoate;

β -[[2-[[[3-[[[(phenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
1,3-benzodioxole-5-propanoic acid;

- 900 -

ethyl β -[[2-[[[3-3-[(phenylamino)carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
1,3-benzodioxole-5-propanoate;

β -[[2-[[[3-3-[(phenylamino)carbonyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-1,3-
benzodioxole-5-propanoic acid;

β -[[2-[[[3-[[[(4-(aminosulfonyl)phenylmethyl]-
amino]carbonyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]pyridine-
3-propanoic acid;

β -[[2-[[[3-[[[(3-pyridinylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

β -[[2-[[[3-[[[(2-carboxyethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

β -[[2-[[[3-[[[(2-phenylethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

β -[[2-[[[3-[[[(1-naphthalenylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-4-
chlorophenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoate;

- 901 -

β -[[2-[[[3-[(aminoiminomethyl)amino]-4-chlorophenyl]carbonyl]amino]acetyl]-amino]benzenepropanoic acid;

β -[[2-[[[5-[(aminoiminomethyl)amino]-2-chlorophenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

ethyl β -[2-[[[3-[[amino(aminocarbonyl)imino]methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[[amino(aminocarbonyl)imino]methyl]amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzene-propanoic acid;

[(dimethylamino)carbonyl]methyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

1,1-dimethylethyl 3,5-dichloro- β -[[2-[[[3[[[(ethoxycarbonyl)amino][(ethoxycarbonyl)imino]methyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

3,5-dichloro- β -[[2-[[[3-[[[(ethoxycarbonyl)amino][(ethoxycarbonyl)imino]methyl]amino]-phenyl]carbonyl]amino]acetyl]-amino]benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-4-chlorophenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoat ;

- 902 -

β -[[2-[[[3-[(aminoiminomethyl)amino]-4-chlorophenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

ethyl 3S-[[2-[[[3-[[amino[(aminocarbonyl)imino]-methyl]amino]phenyl]carbonyl]amino]acetyl]-amino]-4-pentynoate;

3S-[[2-[[[3-[[amino[(aminocarbonyl)imino]-methyl]amino]phenyl]carbonyl]amino]-acetyl]amino]-4-pentynoic acid;

ethyl 3S-[[2-[[[3-[(aminoiminomethyl)-amino]-4-chlorophenyl]carbonyl]amino]-acetyl]amino]-4-pentynoate;

3S-[[2-[[[3-[(aminoiminomethyl)amino]-4-chlorophenyl]carbonyl]amino]acetyl]-amino]-4-pentynoic acid;

(\pm) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,4-dichlorobenzenepropanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3,4-dichlorobenzenepropanoic acid;

(\pm) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)carbonyl]amino]acetyl]amino]-3,4-dichlorobenzenepropanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]-amino]-3,5-dichlorobenzenepropanoic acid;

- 903 -

(±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-2,5-dimethylbenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-2,5-dimethylbenzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-chlorobenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-chlorobenzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-bromobenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-bromobenzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-bromobenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-4-bromobenzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethylbenzenepropanoate;

- 904 -

- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethylbenzenepropanoic acid;
- (±) ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethoxybenzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dimethoxybenzenepropanoic acid;
- (±) (2,2-dimethyl-1-oxopropoxy)methyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;
- (±) β -[[2-[[[3-[[[(aminocarbonyl)imino)-methylamino)methyl]amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminothioxomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3,4-dibromobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-fluoro-5-(trifluoromethyl)benzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-fluorobenzenepropanoic acid;

- 905 -

- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-methylbenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-chlorobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoromethyl)phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-chlorobenzenepropanoic acid;
- (±) [2-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]ethyl] β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-bromo-5-iodobenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-2-hydroxy-4-methoxybenzenepropanoic acid;
- (±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-5-hydroxy-4-methoxybenzofuran-6-propanoic acid;

- 906 -

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-9H-fluorene-2-propanoic acid;

ethyl(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-9H-fluorene-2-propanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-dichloro-2-hydroxybenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2-hydroxy-5-nitrobenzenepropanoic acid;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromo-2-hydroxybenzenepropanoic acid;

ethyl(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dibromo-2-hydroxybenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromo-2-hydroxybenzenepropanoic acid;

ethyl(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromo-2-hydroxybenzenepropanoate;

(±) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-cyclohexanepropanoic acid;

- 907 -

ethyl(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-cyclohexanepropanoate;

ethyl(±) β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichloro-2-hydroxybenzenepropanoate;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-5-chloro-2-hydroxybenzenepropanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3-bromo-5-chloro-2-hydroxybenzenepropanoic acid;

(±) 5-amino-β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-2-hydroxybenzenepropanoic acid;

(±) β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromopyridine-3-propanoic acid;

ethyl(±) β-[[2-[[[3-[(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromopyridine-3-propanoate;

3,5-dichloro-β-[[2-[[[3-[[[(ethoxycarbonyl)amino]-thioxomethyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

3,5-dichloro-β-[[2-[[[3-[[[(ethoxycarbonyl)amino]-iminomethyl]amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

- 908 -

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino][1,1'-
biphenyl]-3-propanoic acid;

1,1-dimethylethyl β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino][1,1'-
biphenyl]-3-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]-
amino]acetyl]amino][pyrimidine-5-propanoic acid;

1,1-dimethylethyl β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
[pyrimidine-5-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]-
amino]acetyl]amino]-3-methylthiophene-2-propanoic acid;

1,1-dimethylethyl β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-3-
methylthiophene-2-propanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3-(methylthio)-
benzenepropanoic acid;

1,1-dimethylethyl (\pm) β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
3-(methylthio)benzenepropanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-6-
methylpyridine-2-propanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3-(methylsulfonyl)-
benzenepropanoic acid;

- 909 -

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-
diethoxybenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]-carbonyl]amino]acetyl]amino]-3,5-
diethoxybenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-
bromothiophene-2-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-
bromothiophene-2-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-5-chlorothiophene-
2-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-5-chlorothiophene-
2-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-1H-pyrazole-
3-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-1H-pyrazole-
3-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-5-methylthiophene-
2-propanoic acid;

- 910 -

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-5-methylthiophen-2-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2,3,5-trichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2,3,5-trichlorobenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2(carboxymethoxy)benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-2(carboxymethoxy)benzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4-methoxy-1,3-benzodioxole-6-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4-methoxy-1,3-benzodioxole-6-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromo-2-methoxybenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-5-bromo-2-methoxybenzenepropanoate ;

- 911 -

β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-6-chloro-1,3-benzodioxole-5-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-6-chloro-1,3-benzodioxole-5-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-benzofuran-2-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-benzofuran-2-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-(carboxymethoxy)benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-phenyl]carbonyl]amino]acetyl]amino]-3-(carboxymethoxy)benzenepropanoate;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4,4,4-trifluorobutanoic acid;

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-4,4,4-trifluorobutanoate;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3-bromo-4,5-dimethoxybenzenepropanoic acid;

- 912 -

thyl(±) β-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3-bromo-4,5-
dimethoxybenzenepropan ate;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-
methylpentanoic acid;

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-
methylpentanoate;

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
phenyl]carbonyl]amino]acetyl]amino]-
pentanoic acid;

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
phenyl]carbonyl]amino]acetyl]amino]-
pentanoate;

β-[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
5-bromo-3-chloro-2-hydroxybenzene-
propanoic acid;

β-[[2-[[[3-[[[(4-pyridinylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]pyridine-3-propanoic acid;

ethyl β-[[2-[[[3-[[[(4-pyridinylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]pyridine-3-propanoate;

3,5-dichloro-β-[[2-[[[3-[[[(4-pyridinylmethyl)-
amino]carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoic acid;

- 913 -

ethyl 3,5-dichloro- β -[[2-[[[3-[[[(4-pyridinylmethyl)-
amino]carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[[[(2-pyridinylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(2-pyridinylmethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate;

3,5-dichloro- β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoic acid;

ethyl 3,5-dichloro- β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

3-chloro- β -[[2-[[[3-[[[(phenylmethyl)amino]-
carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoic acid;

ethyl 3-chloro- β -[[2-[[[3-[[[(phenylmethyl)-
amino]carbonyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[[[(1-phenylethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(1-phenylethyl)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoate;

- 914 -

β -[[2-[[[3-[[[(1H-benzimidazol-2-yl)-methyl]amino]-carbonyl]amino]phenyl]carbonyl]amino]acetyl]-amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-[[[(1H-benzimidazol-2-yl)-methyl]-amino]carbonyl]amino]phenyl]carbonyl]amino]-acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]-amino]carbonyl]amino]phenyl]carbonyl]-amino]acetyl]amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]-amino]carbonyl]amino]phenyl]carbonyl]amino]-acetyl]amino]pyridine-3-propanoate;

3-[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]-amino]carbonyl]amino]phenyl]carbonyl]-amino]acetyl]amino]butanoic acid;

ethyl 3-[[2-[[[3-[[[(3,5-dichlorophenyl)methyl]-amino]carbonyl]amino]phenyl]carbonyl]-amino]acetyl]amino]butanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-bis(1-methylethoxy)benzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-bis(1-methylethoxy)benzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-dibromo-4-hydroxybenzenepropanoic acid;

- 915 -

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dibromo-4-
hydroxybenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dichloro-4-
hydroxybenzenepropanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-3,5-dichloro-4-
hydroxybenzenepropanoate;

β -[[2-[[[5-[(aminoiminomethyl)amino]-2-
hydroxyphenyl]carbonyl]amino]acetyl]amino]-
-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[5-[(aminoiminomethyl)amino]-2-
hydroxyphenyl]carbonyl]amino]acetyl]amino]-
3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[(phenoxyamino)carbonyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(phenoxyamino)carbonyl]amino]-
phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate;

β -[[2-[[[3-[[[(phenylamino)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[[[(phenylamino)amino]carbonyl]-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate;

- 916 -

3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-5-[(3,5-dichlorophenyl)amino]-5-oxopentanoic acid;

ethyl 3-[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-5-[(3,5-dichlorophenyl)amino]-5-oxopentanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxyphenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxyphenyl]carbonyl]amino]acetyl]amino]pyridine-3-propanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxyphenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-[(aminoiminomethyl)amino]-5-carboxyphenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3,5-bis[(aminoiminomethyl)amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3,5-bis[(aminoiminomethyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[(aminoiminomethyl)amino]-5-(trifluoroacetyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

- 917 -

ethyl β -[[2-[[[3-(aminoiminomethyl)amino]-5-(trifluoroacetyl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-(acetylamino)-5-(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

ethyl β -[[2-[[[3-(acetylamino)-5-(aminoiminomethyl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

(\pm) 3,5-dichloro- β -[[2-[[[3-[[(methylamino) (methyylimino) methyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

(\pm) 3,5-dichloro- β -[[2-[[[3-[[(ethylamino) (methyylimino) methyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

(\pm) 3,5-dichloro- β -[[2-[[[3-[[[(1-methylethyl)amino] (methyylimino) methyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

(\pm) β -[[2-[[[3-[[(ethylamino) (methyylimino) methyl]amino]phenyl]carbonyl]amino]acetyl]amino]-4-fluorobenzene-propanoic acid;

(\pm) 4-fluoro- β -[[2-[[[3-[[[(4-pyridinylmethyl)amino] (methyylimino) methyl]amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

- 918 -

β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-4-
fluorobenzenepropanoic acid;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
1H-imidazole-2-propanoic acid;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)amino]phenyl]-
carbonyl]amino]acetyl]amino]-2,3,4,6-
tetrafluorobenzenepropanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
5-bromothiophene-2-propanoic acid;

β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-2-
mercaptobenzenepropanoic acid;

(\pm) β -[[2-[[[3-[(aminoiminomethyl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-5-
chloro-2-mercaptobenzenepropanoic acid;

phenylmethyl β -[[2-[[[3-[(cyanoimino)phenylmethyl-
amino)methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

phenylmethyl β -[[2-[[[3-[(cyanoimino)-
methylamino)methyl]amino]phenyl]carbonyl]amino]-
acetyl]amino]benzenepropanoate;

phenylmethyl β -[[2-[[[3-[(cyanoimino)-
(amino)methyl]amino]phenyl]carbonyl]amino]acetyl]-
amino]benzenepropanoate;

- 919 -

β -[[2-[[[3-[(cyanoimino)(ethylamino)methyl]-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoate;

β -[[2-[[[3-[(cyanoimino)[(phenylmethyl)-amino]methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoic acid;

β -[[2-[[[3-[(cyanoimino)(methylamino)-methyl]amino]phenyl]carbonyl]amino]acetyl]-amino]benzenepropanoic acid;

β -[[2-[[[3-[amino(cyanoimino)methyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

β -[[2-[[[3-[(cyanoimino)(ethylamino)-methyl]amino]phenyl]carbonyl]amino]acetyl]-amino]benzenepropanoic acid;

ethyl 3S-[[2-[[[3-[(cyanoimino)-(methylamino)methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]-4-pentynoate;

3S-[[2-[[[3-[(cyanoimino)(methylamino)-methyl]amino]phenyl]carbonyl]amino]acetyl]-amino]-4-pentynoic acid;

ethyl β -[[2-[[[3-[(cyanoimino)[2-pyridinylmethyl]-amino]methyl]amino]phenyl]carbonyl]amino]-acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[(cyanoimino)[2-pyridinylmethyl]-amino]methyl]amino]phenyl]carbonyl]amino]-acetyl]amino]benzenepropanoic acid;

- 920 -

ethyl β -[[2-[[[3-[[(cyanoimino) [3-pyridinylmethyl]amino]methyl]amino]phenyl]-carbonyl]amino]acetyl]amino]benzenepropanoate;

β -[[2-[[[3-[[(cyanoimino) [3-pyridinylmethyl]-amino]methyl]amino]phenyl]carbonyl]amino]-acetyl]amino]benzenepropanoic acid;

ethyl 3S-[[2-[[[3-[[[(4-(aminosulfonyl)-phenylmethyl]amino)(cyanoimino)methyl]-amino]phenyl]carbonyl]amino]acetyl]-amino]-4-pentynoate;

3S-[[2-[[[3-[[[(4-(aminosulfonyl)phenylmethyl)-amino](cyanoimino)methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]-4-pentynoic acid;

ethyl β -[[2-[[[3-[[amino(cyanoimino)methyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

β -[[2-[[[3-[[amino(cyanoimino)methyl]amino]phenyl]-carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

(\pm) ethyl 3,5-dichloro- β -[[2-[[[3-[(cyanoimino)-(methylamino)methyl]amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoate;

(\pm) 3,5-dichloro- β -[[2-[[[3-[(cyanoimino)(methylamino)-methyl]amino]phenyl]carbonyl]amino]acetyl]-amino]benzenepropanoic acid;

ethyl 3-[[2-[[[3-[[amino(cyanoimino)methyl]amino]-phenyl]carbonyl]amino]acetyl]amino]-4-pentynoate;

- 921 -

(±) ethyl β-[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

(±) β-[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

(±) ethyl β-[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoate;

(±) β-[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-bis(trifluoromethyl)benzenepropanoic acid;

(±) ethyl β-[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]-3,5-dichlorobenzenepropanoate;

(±) β-[[2-[[[3-[(4,5-dihydro-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

(±) ethyl 3,5-dichloro-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoate;

(±) 3,5-dichloro-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]-carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

(±) 3,5-dibromo-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoic acid;

- 922 -

(±) 3-bromo-5-chloro-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]-carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

(±) [2-[2-[2-(2-hydroxyethoxy)-ethoxy]ethoxy]ethyl] 3,5-dichloro-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]-carbonyl]amino]acetyl]amino]benzenepropanoate;

(±) [2-[2-(2-hydroxyethoxy)-ethoxy]ethoxy]ethyl] 3,5-dichloro-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoate;

(±) 3-bromo-5-chloro-2-hydroxy-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

ethyl (±) 3-bromo-5-chloro-2-hydroxy-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoate;

(±) 3,5-dichloro-2-hydroxy-β-[[2-[[[3-[(1,4,5,6-tetrahydropyrimidin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

(±) 3,5-dichloro-β-[[2-[[[3-[(4,5-dihydro-1H-pyrrolidin-2-yl)amino]phenyl]carbonyl]amino]-amino]acetyl]amino]-2-hydroxybenzenepropanoic acid;

- 923 -

(±) 3-bromo-5-chloro-β-[[2-[[[3-[(4,5-dihydro-1H-pyrrolidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-2-hydroxybenzenepropanoic acid;

β-[[2-[[[3-[[5-phenyl-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

ethyl β-[[2-[[[3-[[5-phenyl-1H-imidazol-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoate;

(±) ethyl 3,5-dichloro-β-[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoate;

(±) 3,5-dichloro-β-[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

ethyl (±) 3,5-dichloro-2-hydroxy-β-[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoate;

(±) 3-bromo-5-dichloro-2-hydroxy-β-[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoic acid;

ethyl (±) 3-bromo-5-dichloro-2-hydroxy-β-[[2-[[[3-[(1,4,5,6-tetrahydro-5,5-dimethylpyrimidin-2-yl)amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

- 924 -

(±) ethyl β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

(±) β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoic acid;

(±) ethyl β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-1,3-benzodioxole-5-propanoate;

(±) β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-1,3-benzodioxole-5-propanoic acid;

(±) β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoate;

β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-pyridine-3-propanoic acid;

(±) ethyl β -[[2-[[[4-chloro-3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]-acetyl]amino]pyridine-3-propanoate;

(±) β -[[2-[[[4-chloro-3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]-acetyl]amino]pyridine-3-propanoic acid;

- 925 -

(±) β -[[2-[[[3,5-bis[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]pyridine-3-propanoic acid;

β S-[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]-4-pentynoic acid;

(±) ethyl β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoate;

(±) β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]-3,5-dichlorobenzenepropanoic acid;

(±) ethyl β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)amino]phenyl]carbonyl]amino]acetyl]-amino]-3,5-dichlorobenzenepropanoate;

(±) β -[[2-[[[3-[(3,4-dihydro-2H-pyrrol-5-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-3,5-dichlorobenzenepropanoic acid;

(±) ethyl 3,5-dichloro- β -[[2-[[[3-[(2,3,4,5-tetrahydropyridin-6-yl)amino]phenyl]carbonyl]amino]acetyl]amino]benzenepropanoate;

(±) 3,5-dichloro- β -[[2-[[[3-[(2,3,4,5-tetrahydropyridin-6-yl)amino]phenyl]carbonyl]-amino]acetyl]amino]benzenepropanoic acid;

(±) 3,5-dichloro-2-hydroxy- β -[[2-[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)-amino]phenyl]carbonyl]amino]acetyl]amino]-benzenepropanoic acid;

- 926 -

ethyl(±) 3,5-dichloro-2-hydroxy-β-[[2-
[[[3-[(3,4,5,6-tetrahydro-2H-azepin-7-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
benzenepropanoate;

(±) ethyl β-[[2-[[[3-[(iminophenylmethyl)-
amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoate;

βS-[[2-[[[3-[[imino(1-pyrrolidinyl)methyl]-
amino]phenyl]carbonyl]amino]acetyl]-
amino]-4-pentynoic acid;

(±) β-[[2-[[[3-[(iminophenylmethyl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

3,5-dichloro-β-[[2-[[[3-[[imino(1-
piperidinyl)methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]benzenepropanoic acid;

ethyl 3,5-dichloro-β-[[2-[[[3-[[imino(1-
piperidinyl)methyl]amino]phenyl]carbonyl]-
amino]acetyl]amino]benzenepropanoate;

ethyl β-[[2-[[[3-[(4,5-dihydrothiazol-2-
yl)amino]phenyl]carbonyl]amino]acetyl]-
amino]pyridine-3-propanoate;

β-[[2-[[[3-[(4,5-dihydrothiazol-2-yl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

β-[[2-[[[3-[[benzoxazol-2-yl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

- 927 -

ethyl β -[[2-[[[3-[[benzoxazol-2-yl)amino]-
phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate.

β -[[2-[[[3-[(5,6-dihydro-4H-thiazin-2-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoic acid;

and

ethyl β -[[2-[[[3-[(5,6-dihydro-4H-thiazin-2-yl)-
amino]phenyl]carbonyl]amino]acetyl]amino]-
pyridine-3-propanoate.

43. A method according to Claim 41 wherein the condition treated is tumor metastasis.
44. A method according to Claim 42 wherein the condition treated is tumor metastasis.
45. A method according to Claim 41 wherein the condition treated is solid tumor growth.
46. A method according to Claim 42 wherein the condition treated is solid tumor growth.
47. A method according to Claim 41 wherein the condition treated is angiogenesis.
48. A method according to Claim 42 wherein the condition treated is angiogenesis.
49. A method according to Claim 41 wherein the condition treated is osteoporosis.
50. A method according to Claim 42 wherein the condition treated is osteoporosis.

- 928 -

51. A method according to Claim 41 wherein the condition treated is humoral hypercalcemia of malignancy.
52. A method according to Claim 42 wherein the condition treated is humoral hypercalcemia of malignancy.
53. A method according to Claim 41 wherein the condition treated is smooth muscle cell migration.
54. A method according to Claim 42 wherein the condition treated is smooth muscle cell migration.
55. A method according to Claim 53 wherein restenosis is inhibited.
56. A method according to Claim 54 wherein restenosis is inhibited.
57. A method according to Claim 41 wherein the condition treated is rheumatoid arthritis.
58. A method according to Claim 42 wherein the condition treated is rheumatoid arthritis.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/13500

A. CLASSIFICATION OF SUBJECT MATTER

| | | | | | |
|-------|------------|------------|------------|------------|------------|
| IPC 6 | C07D213/55 | A61K31/44 | C07C279/18 | A61K31/155 | A61K31/36 |
| | C07D405/10 | A61K31/395 | C07D223/12 | C07D401/14 | C07D207/16 |
| | C07C275/28 | A61K31/17 | C07D401/10 | C07D317/30 | |

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D A61K C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | EP 0 445 796 A (F.HOFFMANN-LA ROCHE) 11 September 1991 see page 7, line 37 - line 40; claim 1 --- | 1-58 |
| E | WO 96 26190 A (SMITHKLINE BEECHAM) 29 August 1996 see claim 1 --- | 1-58 |
| P,A | WO 96 00574 A (SMITHKLINE BEECHAM) 11 January 1996 see claim 1 --- | 1-58 |
| A | EP 0 643 072 A (TAKEDA) 15 March 1995 see claim 1 --- | 1-58 |
| A | WO 94 18981 A (MERCK & CO.) 1 September 1994 see page 28, line 22; claim 1 ----- | 1-58 |

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

Date of the actual completion of the international search

10 December 1996

Date of mailing of the international search report

23.01.1997

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+ 31-70) 340-3016

Authorized officer

Gettins, M

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 96/13500

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|----------------------------|---------------------|
| EP-A-445796 | 11-09-91 | CA-A- 2037153 | 10-09-91 |
| | | IL-A- 97401 | 15-03-95 |
| | | JP-B- 2501252 | 29-05-96 |
| | | JP-A- 4217652 | 07-08-92 |
| | | US-A- 5430024 | 04-07-95 |
| | | US-A- 5273982 | 28-12-93 |
| | | HR-A- 930353 | 30-06-96 |
| ----- | | | |
| WO-A-9626190 | 29-08-96 | NONE | |
| ----- | | | |
| WO-A-9600574 | 11-01-96 | AU-A- 3001095 | 25-01-96 |
| | | WO-A- 9600730 | 11-01-96 |
| ----- | | | |
| EP-A-643072 | 15-03-95 | AU-A- 6477194 | 22-12-94 |
| | | CA-A- 2126026 | 18-12-94 |
| | | CN-A- 1098409 | 08-02-95 |
| | | FI-A- 942881 | 18-12-94 |
| | | HU-A- 70045 | 28-09-95 |
| | | JP-A- 7157472 | 20-06-95 |
| | | NO-A- 942274 | 19-12-94 |
| | | US-A- 5550131 | 27-08-96 |
| ----- | | | |
| WO-A-9418981 | 01-09-94 | AU-A- 6246594 | 14-09-94 |
| | | BG-A- 99863 | 29-02-96 |
| | | CA-A- 2155123 | 01-09-94 |
| | | CN-A- 1118139 | 06-03-96 |
| | | CZ-A- 9502108 | 14-02-96 |
| | | EP-A- 0684823 | 06-12-95 |
| | | FI-A- 953916 | 21-08-95 |
| | | HU-A- 71796 | 28-02-96 |
| | | JP-T- 8507072 | 30-07-96 |
| | | NO-A- 953270 | 19-10-95 |
| | | PL-A- 310386 | 11-12-95 |
| ----- | | | |